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Lesions of uncertain malignant potential (B3) on core biopsy in the NHS Breast Screening Programme: is the screening round relevant?

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ABSTRACT

INTRODUCTION Most women who have screening mammography and undergo subsequent open biopsy following an indeterminate core biopsy result are eventually found to have benign disease. However, a significant number have malignant disease and the rate of malignancy in such cases may be influenced by various factors. This study examined the effect of the type of screening round (prevalent or incident) on the likelihood of breast cancer being present.

METHODS A total of 199 women who had NHS breast screening mammograms and subsequent indeterminate (B3) core biopsy results followed by excision biopsy over an 11-year period in a single breast screening unit were reviewed.

RESULTS The rate of malignancy following excision of a lesion graded as B3 on core biopsy was 21% for women in the prevalent screening round compared to 33% in subsequent rounds (Fisher's exact test, p=0.038).

CONCLUSIONS The incidence of malignancy associated with a B3 core biopsy result appears to be related to the screening round in which the lesion is detected, being approximately 50% higher in the subsequent incident rounds compared to the initial prevalent round. This finding may be useful in formulating management plans for women who have an indeterminate biopsy result.

KEYWORDS

Breast cancer – Screening – Needle biopsy

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Over two million women underwent screening mammography in the NHS Breast Screening Programme (NHS BSP) in 2008–2009.[1] An important aim of this screening programme is to maximise the non-operative diagnosis rate,[2] establishing a diagnosis of breast cancer by core biopsy or cytological means prior to definitive surgery. Just over 0.1% of all women screened by the NHS BSP undergo an open biopsy to allow definitive histological diagnosis of a screen detected lesion.[1] Of those undergoing diagnostic open biopsy, almost 70% are found to have benign disease. The NHS BSP also aims to minimise the number of open biopsies that prove to be entirely benign in order to contain the costs of the programme and to limit patient anxiety associated with false positive results.[3]

A core biopsy graded as B3 (lesion of uncertain malignant potential)4 for screen detected lesions can prove difficult to manage. Options for further management include repeat core biopsy and diagnostic open (surgical) biopsy. Most women in this situation will ultimately have benign breast disease but some will have high risk lesions such as atypical ductal hyperplasia (ADH) and atypical lobular hyperplasia (ALH). However, in situ or invasive malignancy is found in up to a third of cases.[5–7]

We aimed to determine the rate of malignancy at open biopsy in lesions where a preoperative B3 result had been obtained and whether this rate varied according to the type of screening round. If the incidence of malignancy is related to the screening round, this may help guide the management of patients with a B3 core biopsy result.

Methods

All women invited by the West Devon and East Cornwall breast screening unit who had screening mammograms and a subsequent B3 core biopsy from January 1999 to December 2009 were identified and a retrospective review was performed. A total of 235 cases were identified. In each case, the core biopsy result was reviewed along with the final histology result after open biopsy. The screening records of those women who did not undergo subsequent open biopsy were also reviewed. In all cases, individual patient manage-

Table 1 Summary of histology results following excision biopsy in 199 patients having had a B3 core biopsy result

Histology following surgical biopsy	Prevalent round	Incident rounds	Total
Benign	58	84	**142**
Malignant	15	42	**57**
Total	**73**	**126**	**199**

Table 2 Number of cases of each type of cancer diagnosed at surgical biopsy for the incident and prevalent screening rounds

Histological diagnosis following surgical biopsy	Prevalent round	Incident rounds
Ductal carcinoma in situ	9	21
Lobular carcinoma in situ	3	11
Invasive ductal cancer (no special type)	1	8
Tubular carcinoma	0	2
Papillary carcinoma	1	0
Invasive lobular carcinoma	1	0
Total malignant lesions	**15**	**42**

Table 3 Number of cases of benign lesions present in open surgical biopsies for the incident and prevalent screening rounds

Histological diagnosis following surgical biopsy	Prevalent round	Incident rounds
Complex sclerosing lesion / radial scar	17	21
Atypical lobular hyperplasia	1	1
Atypical ductal hyperplasia	5	5
Columnar cell change	6	7
Benign cyst	0	1
Papilloma	8	29
Ductal hyperplasia	0	3
Benign phyllodes tumour	5	3
Epithelial hyperplasia	4	3
Fibroadenoma	6	5
Fibrocystic change	3	2
Focal lactational change	0	1
Sclerosing adenosis	2	1
Hamartoma	1	1
No discrete lesion seen	0	1
Total benign lesions	**58**	**84**

ment had been discussed and agreed at the unit's weekly multidisciplinary team meeting.

Results

Of the 235 women who were initially identified, 27 (11%) did not have their lesion excised. Their mean age was 50.4 years (range: 49–52 years). Overall, 208 women (89%) underwent open surgical biopsy although 9 cases did have further intervention before their surgical procedure. The mean age of these women was 57.6 years (range: 49–79 years) (Mann–Whitney U test, $p<0.0001$).

Six women underwent repeat core biopsy, which supported the original B3 diagnosis, and then proceeded to excision biopsy. One woman underwent a mammotome biopsy that upgraded the B3 result to B5a and then underwent therapeutic excision. One woman had therapeutic mammotome excision of her papilloma and a further patient had mammotome core biopsy prior to excision of a complex sclerosing lesion. These nine patients were excluded from further analysis, leaving 199 women who underwent diagnostic open biopsy as their next investigation. These formed the cohort for the main study.

Of 27 women who did not have their lesion excised, 19 have re-entered the breast screening programme and have had subsequent normal mammograms. Two have re-entered the programme but have yet to be screened again. Four women declined further screening and two have been lost to follow up. The mean follow-up duration was 49 months (range: 5–135 months). To date none of these women have been found to have subsequent malignancy.

Of the 199 women undergoing open biopsy, 73 (37%) were in the prevalent screening round and 126 (63%) in the incident rounds (Table 1). Of the 73 women identified during the prevalent round of screening, 15 (21%) had malignancy. In the incident rounds, 42 (33%) had a malignant diagnosis (Fisher's exact test, $p=0.038$). The mean ages in the prevalent and incident rounds were 50.6 years (range: 48–53 years) and 61.5 years (range: 53–79 years) respectively (Mann–Whitney U test, $p<0.0001$).

The 19 women who have been re-imaged and have had normal mammography have not been included in this calculation. They were all in the prevalent round and their addition to the prevalent round figures would make the final malignant diagnosis in that group 16% and the difference between the groups more marked (Fisher's exact test, $p=0.0033$).

Of the 199 women who had their lesion excised, malignancy was found in 57 (29%). Of these, 44 cancers (77%) were either ductal carcinoma in situ ($n=30$) or lobular carcinoma in situ ($n=14$). The excision biopsies that revealed malignant disease and the final histological diagnosis are shown in Table 2.

There were non-malignant diagnoses in 142 women, representing a wide spectrum of benign breast conditions. In addition, several high risk lesions were identified (Table 3). There were 17 complex sclerosing lesions/radial scars in the prevalent round, representing 23% (17/73) of all B3

biopsies compared to 17% (21/126) in the incident rounds (Fisher's exact test, p=0.17).

Discussion

A minority of assessments following mammography in symptomatic women or a screened population yield an indeterminate core biopsy result[6] but further management in such cases can prove difficult. Approximately 5% of all core biopsies for screen detected breast lesions produce a B3 result.[5,7] The rates of indeterminate core biopsy vary with the patient population and are higher in screen detected than in symptomatic patients.

Excision biopsy is undertaken in most cases to exclude malignant disease, with open biopsy rates of 80–90% reported.[5,7] In the current series, 89% of women proceeded directly to open biopsy. A few had repeat core biopsies with the remainder having no further intervention other than routine screening mammography. Multidisciplinary discussion and appropriate risk assessment are essential to optimise patient management and long-term follow up is required to ensure the safety of this policy in selected cases. The current study does not have sufficient numbers or adequate follow-up data to provide any reliable guidelines for not performing excision biopsy when an indeterminate result has been achieved.

A significant rate of malignancy, especially non-invasive disease, is seen in women who have an indeterminate core biopsy after screening mammography. Reported rates of malignancy at open biopsy vary from 21%[6] to 34%.[7] The rate in the current series of 29% lies within this range. In our series, two-thirds of all cancers were in situ, the same proportion as reported by another NHS breast screening unit in 2008[7] and similar to the value of 57% reported from Nottingham.[5] Preoperative diagnosis of in situ cancer is more difficult than for invasive cancers.[1] Such differences would explain the higher percentage of in situ disease in patients with an indeterminate core biopsy compared to the total population of women diagnosed with screen detected breast cancer. The ratio of invasive to in situ disease in this latter group has remained relatively stable in the NHS BSP at approximately of 4:1 over the last ten years.[1]

Histological features, such as a papillary lesion with atypia[8] and lobular neoplasia[6] have been shown to be associated with higher rates of malignancy, especially if pleomorphic lobular carcinoma in situ is present on core biopsy.[9] In such cases, rates of malignancy following open biopsy may be as high as 40–60%. In contrast, a papillary lesion with no atypia seen on core biopsy has a less than 5% chance of malignancy.[5] Although these figures are useful, a reliable method of determining which patients do not require excision is not yet available. A predictive tool that includes all relevant factors that might indicate the risk of malignancy being present would be valuable in such circumstances.

Differential rates of malignancy according to the type of screening round may help manage women with B3 core biopsy results and who have not been previously examined. The current study indicates that a lesion of uncertain malignant potential in incident screening rounds is 50% more likely to be malignant than in the first (prevalent) round. As breast cancer is more common with increasing age, women in the later screening rounds would be expected to have a higher rate of breast cancer due to their older age. The age specific incidences for breast cancer for women aged 50–54 and 60–64 are 262/100,000 per year and 342/100,000 per year respectively.[10] These age groups approximate to the ages of the women in the prevalent and incident rounds in the current study. The higher proportion of malignancies in the incident group was greater than could be accounted for by the age specific incidences.

Conclusions

Accurate biopsy results are necessary for appropriate management of breast cancer. Techniques to further increase the preoperative diagnosis rate would obviate the need for multiple surgical procedures. Needle core biopsy underestimates the presence of malignant disease when high risk lesions such as ADH, ALH and lobular carcinoma in situ are present.[11,12] Core biopsy may not detect foci of malignancy in benign tissue, especially if the foci are small. Using a smaller core needle or taking four or fewer core biopsy samples is associated with a risk of underdiagnosing breast cancer.[11,13] Increasing the volume of tissue excised by using larger gauge needles,[11] vacuum assisted devices[12] or newer basket techniques may facilitate accurate preoperative diagnosis. Further evaluation is required to assess the potential role of these devices as previous studies have been retrospective and non-randomised.

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