

changed to IDC after surgery, the pre-operative core biopsy specimens were reviewed.

**Results:** Of 160 pre-operative core biopsies, 17 (10.6%) showed DCIS, 110 IDC, 20 lobular invasive carcinoma and 16 had other cancers. The final pathological diagnoses were: DCIS 13 (8.1%), IDC 107 (66.9%), invasive lobular carcinoma 19 (11.9%), others 21 (13.1%). Four (23.5%) of those diagnosed as DCIS on core biopsy turned out to contain IDC. In all four cases the tumors were palpable, with a diameter of 10 mm or more. In 56 (52%) cases with IDC grade was not determined on the core biopsy specimen. Of those 51 (48%) in which grade was determined, there was a discrepancy of up to 2 grades between pre-operative and surgical pathology reports in 5 (9.8%) of the cases. In only 1 of the 5 tumors with vascular or lymphatic invasion was the information available from the core biopsy.

**Conclusions:** Information obtained from core biopsies regarding tumor type and grade is often incomplete. One quarter of tumors diagnosed as DCIS are subsequently found to include an invasive component (all palpable in our series). Even when the diagnosis of IDC is made on core biopsy, there is frequently a discrepancy in assessment of tumor grade or lymphovascular invasion. Since information from diagnostic core biopsies is crucial in decision-making for sentinel lymph node biopsy and the emerging technology of tumor ablation, the possibility of a discrepancy between findings in core biopsies and surgical specimens should be taken into account in patient selection and efforts should be made to reach a more accurate pre-operative diagnosis.

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POSTER

#### **Histological core needle biopsy of palpable breast lesions: image guided or palpation guided**

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**Purpose:** Histological core needle biopsy of palpable breast lesions can be performed either by image guidance (stereotactic or ultrasonographic) or by palpation guidance. The purpose of this study is to determine differences in diagnostic performance of the histological core needle biopsy obtained by different kinds of guidance techniques.

**Patients and methods:** Retrospectively a group of patients with a palpable breast lesion who underwent a histological core needle biopsy was studied. Between January 1999 and July 2002 239 women with 267 palpable breast lesions (mean age of 53.0 years) underwent a histological core needle biopsy, because of non-conclusive triple diagnostic tests. The choice for a free hand or an image-guided technique was mainly influenced by logistic reasons such as a long waiting list for a radiological appointment. The histology of the core needle biopsy was compared with the findings at excision (216), or follow-up (51).

**Results:** The histological core needle biopsy was performed on palpation in 58 cases and by image guidance in 209 cases (ultrasonography in 167 cases and stereotactic in 42 cases). The mean size of the palpable breast lesions biopsied by palpation was significant larger. Seven times the result of the histological core needle biopsy was inconclusive (twice at palpation, five times by imaging). Histological core needle biopsy by palpation showed a sensitivity of 0.71 and a specificity of 0.93. Biopsy by image guidance (although smaller in size) showed a better sensitivity (0.93,  $p < 0.001$ ) and specificity (0.99,  $p = 0.057$ ).

**Conclusion:** Free-handed histological core needle biopsy of a palpable breast lesion has an insufficient diagnostic performance compared to an image guided technique. Size seems a pitfall for physicians to perform a histological core needle biopsy free-handed and not by image guidance. Once a histological core needle biopsy is indicated it should be performed by image guidance. The organisation of diagnostic procedures should be adjusted to this accordingly.

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#### **Clinically and mammographically occult breast lesions at MR Imaging: potential impact of computerized assessment on clinical reading**

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**Purpose:** To investigate whether computerized analysis of clinically and mammographically occult breast lesions at MR imaging complements

clinical reading, how it complements clinical reading, and to assess the potential impact of the system.

**Material and methods:** An existing computerized analysis system was enhanced by training on 100 breast lesions and validating on 136 independent lesions. Seventy-five lesions in the training were also graded in daily clinical practice. These grades (5-point scale: benign, probably benign, indeterminate, suspicious, highly suggestive of malignancy) and the probability of malignancy calculated by computerized analysis were entered as covariates in logistic regression analysis to obtain a combined model. The performance of the model was compared with that of clinical reading alone in order to provide guidelines when and by how much computerized analysis is able to complement clinical reading. For this purpose, an independent set of 72 clinically and mammographically occult lesions was read in clinical setting, and assessed by the combined model.

**Results:** The performance of reading in clinical setting ( $A_z = 0.86$ ) was similar to that of the computerized analysis ( $A_z = 0.85$ ;  $p = 0.99$ ). A significant improvement was obtained by the combined model ( $A_z = 0.91$ ;  $p = 0.03$ ). Improvement was mostly accomplished for lesions graded indeterminate and suspicious by the radiologists. In the combined model, an increase in specificity of approximately 20% was observed without reduction of sensitivity.

**Conclusions:** Computerized analysis complements clinical reading, making computer-aided diagnosis feasible. The complementary information has the potential to increase the specificity for clinically and mammographically occult lesions without reducing sensitivity.

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#### **The 2001/02 ABS at BASO Audit – repeat therapeutic operations and pre-operative history**

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The 2001/02 ABS at BASO audit included 10,191 cancers detected by the UK NHSBSP between 1 April 2001 and 31 March 2002. 93% of invasive cancers and 73% of non-invasive cancers had a pre-operative diagnosis. 98% of B5b (Invasive) cancers and 92% of C5 cancers had surgical confirmation of invasive cancer. 470 (25%) B5a (Non-invasive) cancers were found to be invasive following surgery. 97% of B5b (Invasive) and C5 cancers had known nodal status whereas only 84% of B5a (Non-invasive) cancers had known nodal status.

Overall, 14% of invasive cancers and 20% of non-invasive cancers underwent more than one surgical operation. 41% of the B5a (Non-invasive) cancers had repeat operations; 34% involving axillary procedures. In one UK region, 97% of B5a (Non-invasive) cancers had known nodal status, 54% being determined on the basis of repeat operations involving the axilla. Screening units within this region thus have a policy of returning to obtain nodes following the unexpected discovery of invasive disease following surgery. In two UK regions, where the proportion of B5a cancers with nodal status was between 70% and 71%, repeat operation rates were lower than in other regions (27% and 30% respectively). It would therefore appear that there is an unwillingness in these regions to carry out a repeat operation to determine the nodal status and that as a result, a proportion of women may have been under diagnosed.

Overall, 7.1% of invasive cancers with a C5 pre-operative diagnosis had their nodal status determined as a result of axillary procedures undertaken as repeat operations. In one UK region, without these additional axillary procedures, the proportion of cancers in this group with known nodal status would have been 66% rather than 87%. It would thus appear that in this UK region there is a reluctance to carry out an axillary nodal procedure at the first operation for cancers diagnosed pre-operatively by cytology alone, and that repeat operations are subsequently undertaken for a high proportion of invasive C5 cancers in order to determine the nodal status.

**The 2001/02 ABS at BASO audit data thus demonstrate clear differences in the treatment protocols followed within the UK NHSBSP.**

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#### **Impact of random variations in the measurements of tumor extent on the WHO and the RECIST guidelines for solid breast tumors**

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**Purpose:** To quantify the fraction of false-positive calls on tumor regression and tumor progression using the WHO and the RECIST guidelines for solid

breast tumors as a consequence of random variations in the measurements of tumor size.

**Materials and Methods:** Unidimensional measurements (largest diameter, RECIST) and bidimensional measurements (product of largest diameter and its perpendicular, WHO) of tumor extent were performed on 159 lesions in breast cancer patients, using mammography, ultrasonography, and MRI. The random variations in these measurements were quantified using an analysis of variance technique, and were used to predict the fraction of false-positive calls for tumor regression and the fraction of false-positive tumor progressions that result from employing the WHO and the RECIST guidelines for monitoring tumor response to neoadjuvant treatment.

**Results:** Using the WHO criteria, the estimated fraction of false-positive calls for tumor regression is 13% (mammography), 10% (ultrasonography), and 13% (MRI). For tumor progression, the estimated fraction of false-positive calls is 29% (mammography), 26% (ultrasonography), and 28% (MRI). Employing the RECIST criteria results in an estimated fraction of false-positive calls for tumor regression of 13% (mammography), 12% (ultrasonography), and 11% (MRI). For tumor progression, the estimated fraction of false-positive calls is 23% (mammography), 22% (ultrasonography), and 19% (MRI).

**Conclusions:** Both the WHO and the RECIST guidelines overestimate tumor regression and tumor progression. In particular, tumor progression may be considerably overestimated, although somewhat less by the RECIST than by the WHO guidelines. If a lower fraction of false-positive calls is desired in monitoring the response of solid breast tumors to neoadjuvant treatment, the criteria may need to be refined using quantitative knowledge of the reproducibility in the measurements of tumor extent.

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# **Six-year experience of equivocal (B3) and suspicious (B4) breast core biopsies from screen-detected lesions: correlation with radiology, cytology and final excision**

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**Background:** To review our experience with equivocal and suspicious results on breast core needle biopsies (CNB) from screen-detected lesions between 01/07/1997 and 30/06/03.

**Methods:** The data were extracted from the National Health Service Breast Screening Programme (NHSBSP) screening office computer, cytology files and histopathology database. Radiology, Fine Needle Aspiration Cytology (FNAC) and CNB were reported according to the guidelines of the NHSBSP. B3/B4 CNBs were correlated with pre-operative Radiological and FNAC findings and subsequent pathology excision results.

**Results:** During the study period, 915 CNBs were received from screen-detected lesions. 70 (7.7%) were reported B3 and 40 (4.4%) were reported B4. 109/110 of the B3/B4 CNBs had concurrent FNAC. The radiological risk score was available for all 110 cases. 103/110 (93.6%) had excision biopsy (all histology reports available); the remaining 7 patients have radiological follow-up available for a mean of 45 months (range 12–75). The Positive Predictive Value for malignant histology on excision (PPV) of B4 was 87.5% and the PPV of B3 was 36%.

All B4 cases were excised and the 5 benign B4 CNB were derived from atypical ductal hyperplasia (ADH). The 38 cases with B3 CNB and a benign excision biopsy included ADH (6), radial scar/complex sclerosing lesion (18), atypical lobular hyperplasia (1), granular cell tumour (1), myofibroblastoma (1), Phyllodes tumour (1), papilloma (3), fibrocystic change (3), fibroadenoma (1), sclerosing adenosis (1), pseudoangiomatous stromal hyperplasia (1), and normal breast tissue (1).

During the study period, 2615 FNAC were performed on screen-detected lesions. FNAC statistics of this cohort of FNAC indicate a 59% absolute sensitivity for FNAC with a PPV of 99.8% for C5 cytology and 85.3% for C4 cytology. We had no C5 FNAC among the 25 cancers with B3 CNB. Only 14 of the 35 cancers with B4 CNB had a C5 FNAC.

**Conclusions:** There have been fears that the B3 category may lead to an increase in the benign biopsy rate, but our data support excision of lesions with B3 at CNB. There are no Mammotome biopsies in this study but this may be a viable second line of investigation. We speculate that cancers with a B3 or B4 CNB may be a sub-group in which it is difficult to obtain a pre-operative diagnosis by any diagnostic modality as the FNAC results in this subset are at variance with our overall cytology results. Excision is mandatory for any case with a B4 diagnosis.

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# **Breast duct micro-endoscopy does not diagnose pre-invasive malignancy**

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**Introduction:** We have previously demonstrated the feasibility of breast duct micro-endoscopy. We describe the early results of this technique when used to investigate nipple discharge.

**Procedure:** Duct endoscopy was carried out using micro endoscopes between 0.5 mm and 1.1 mm external diameter. (Polydiagnost GmbH). For the first time a micro-cytology brush was used to obtain samples in addition to duct aspirates.

**Results:** 28 patients were investigated, 20 had unilateral single duct discharge (16/20 bloodstained), and 8 unilateral multi-duct discharge (3/8 bloodstained). 12 cases were carried out under local anaesthesia. Good visualisation of the discharging ducts was achieved in 100% of cases to a maximum depth of 7.5 cm, (median depth 5.2 cm). A maximum of 8 duct bifurcations (median 3) were crossed during the examinations. We identified pathology in 15 patients (single papilloma in 6, multiple papilloma in 2, duct adhesions 2, inflammation in 5, obstructed duct in 2, foreign body in 1). 2 patients also had nipple aspirate cytology examined and 1 of these yielded cells. 4 had cytology by micro-brush, and 3 provided sufficient cells for analysis. All cases subsequently underwent excisional surgery. The findings on endoscopy were in agreement with the pathology in 20 cases. Endoscopy failed to diagnose papillomas in 4 cases where the lesions were in adjacent, non-discharging ducts. In 1 case multiple papillomas were seen but histology suggested that these were polypoid granulomas. Cytology (aspirate) showed papillary fragments. Cytology was in agreement with the histology in 3/4 cases. However, DCIS was diagnosed on histology in one case, DCIS/LCIS in one case and ADH in another. None of these 3 cases had visible macroscopic abnormalities within the discharging duct on endoscopy. Cytology was available in 1 of these patients (aspirate and micro-brush) but this provided insufficient cells for diagnosis (C1).

**Conclusion:** Breast duct micro-endoscopy provides clear pictures of the discharging ducts to a greater depth than would usually be removed at surgery. Papillomas in adjacent ducts can be missed but these are probably not contributing to the discharge. In this small series breast duct micro-endoscopy on its own is not sufficient to diagnose pre-invasive malignancy.

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# **The role of axillary nodal staging during preoperative breast diagnostics**

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The ultrasonographic work-up of the axilla is part of the examination of the breast. This permits an imaging assessment of axillary nodal status and offers guidance for fine needle aspiration (FNA) of visualized lymph nodes (LNs). The presence and demonstration of metastatic LNs obviates the need for sentinel lymph node (SLN) biopsy even in the event of non-palpable axillary LNs.

During a period of 6 months, there were 64 patients who had axillary FNA cytology (FNAC) from enlarged LNs. LNs were categorised either as reactive or pathological by ultrasound (US). LNs were classified as pathological if they had an even or uneven enlargement of the cortical area, had a central area that had become hypoechogenic, or had become rounded. US-guided sampling was done from the cortical area of the LNs.

Of the 37 cases categorised as pathological by US, FNAC was reported as inadequate in 5, and as negative for metastasis in 8. Eleven patients had no axillary surgery either because of primary chemotherapy or because of negative breast imaging findings and FNAC of the axillary LN, whereas 26 patients had either diagnostic excision of the LN, or SLN biopsy or axillary dissection; 21 had metastatic disease in the axilla, 2 had nodal involvement by lymphoma, 1 had tuberculous lymphadenitis, and 2 patients had no relevant nodal pathology. Three inadequate and 3 negative FNAC specimens were found to have metastasis in the axilla; the tuberculous lesion and one of the lymphomas were reported as inadequate and negative, respectively. Of the 27 cases categorized as reactive by US, 8 were reported as inadequate, 1 as metastatic and the remaining as non metastatic by FNAC. Eleven patients had some type of axillary surgery, 8 had metastatic nodal involvement, and 1 had nodal involvement by a lymphoma. The sensitivity and specificity of axillary US to detect metastatic