O-118. Breast carcinomas with basal/myoepithelial differentiation: a review of morphology and immunophenotypical analysis

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This study assessed the morphological characteristics and immunohistochemical (IHC) profile of breast carcinomas with basal and myoepithelial phenotype. We examined 1870 cases of invasive breast carcinoma, using tissue microarrays and IHC, to identify tumours showing basal/myoepithelial phenotype. Tumours were classified into 2 groups; 1) tumours with basal phenotype [expressing ck5/6 and/or ck14]; 2) tumours with myoepithelial phenotype (expressing actin and/or p63). Group 1 was further divided into two subgroups; A) dominant basal pattern [10–50% of cells are positive]; B) basal characteristics [≤50% of cells are positive]. GrouplA tumours constituted 10%; grouplB 8.6% and group2 constituted 13.7% of the cases. The majority of these tumours were grade 3. There were positive associations with the adenoid cystic growth pattern, loss of tubular formation, marked cellular pleomorphism, poorer NPI, development of distant metastasis. Associations were found with loss of expression of hormone receptors, neuroendocrine markers, BRCA1 and Fhit proteins and positive expression of p53, EGFR, p-cadherin. No association with vascular invasion was found. The commonest histological types were ductal/no special type, medullary like, mucinous and adenoid cystic growth pattern. The most common morphological characters of group 1 were bigger size, high-grade comedo-type necrosis and adenoid cystic pattern, positive lymph node disease and development of tumour recurrence. Group2 was noticed in younger age group and associated with central necrosis/fibrosis, basaloid cell change, positive e-cadherin, cerbb4. Group1 showed a strong negative association with both overall survival (OS) (Log Rank(LR) = 22.5, $p < 0.001$) and disease free interval (DFS) (LR = 30.1, $p < 0.001$) while group 2 showed an association with as (LR = 5, $p = 0.02$) but not with DFS. Multivariate analysis showed that basal but not myoepithelial phenotype has an independent value in predicting outcome.

O-119. A review of the pathological features of 86 LCIS cases – to determine diagnostic accuracy

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Background: Pathologically Lobular carcinoma in situ (LCIS) can cause diagnostic dilemmas.

Aims: To find ways of improving the accuracy of pathological diagnosis of LCIS.

Methods: 59 screening centres in England provided data on all cases of screen detected LCIS. Original blocks and slides were requested on all cases. Histological assessment involved H&E stain, E-cadherin, Cytokeratin 5/6 and 34B E12, and a mucin stain. We investigated differences in survival rates.

Results: 366 cases of LCIS were identified, of which the pathology has been reviewed on 86 so far. 66 were found to be LCIS, 15 DCIS, 1 ADH, 3 sclerosing adenosis and 1 invasive carcinoma. Of these 86, 72 diagnoses were made confidently on H&E stain alone and confirmed with immunohistochemistry, the remaining 14 diagnoses were classified as equivocal on H&E stain and the diagnosis relied more on immunohistochemistry. The immunohistochemistry results are listed in Table 1.

Table 1

	E-Cadherin		CK 5/6		34B E12		Mucin	
	Dcis	Lcis	Dcis	Lcis	Dcis	Lcis	Dcis	Lcis
Negative	0	61	15	63	10	7	8	4
Equivocal	1	3	0	0	3	8	3	5
Positive	14	0	0	1	2	49	3	55
Unknown	0	2	0	2	0	2	0	2

Tumour free survival in women with radial scars was 3.52/1000 women years compared with 20.97/1000 women years for those without radial scars; RR 0.17 (CI95 0.02=-1.25; $p = 0.08$).

Conclusions: In the majority of cases LCIS can be detected solely on H&E stain. To improve diagnostic accuracy of LCIS, E-cadherin, 34B E12, and mucin stains should be considered.

O-120. Measurement of large scale genomic instability is an excellent prognostic tool in ductal carcinoma in situ

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Gross genomic aberrations are increasingly seen as a cause rather than a consequence of carcinogenesis. Early evidence suggest such aberrations may serve as accurate prognostic and moreso predictive markers in precancerous lesions such as DCIS. Additionally, identification of high risk patients may be useful in the selecting candidates for chemoprevention trials or additional adjuvant therapy.

75 patients with an initial diagnosis of DCIS were used in this study, 50 with no evidence of relapse and 25 who developed a recurrence. Genomic instability was measured by a novel method of DNA ploidy and nucleotyping employing texture analysis, image cytometry and computational analysis.

Results demonstrated that nucleotyping with this novel technique showed an excellent prediction of recurrence in these patients.

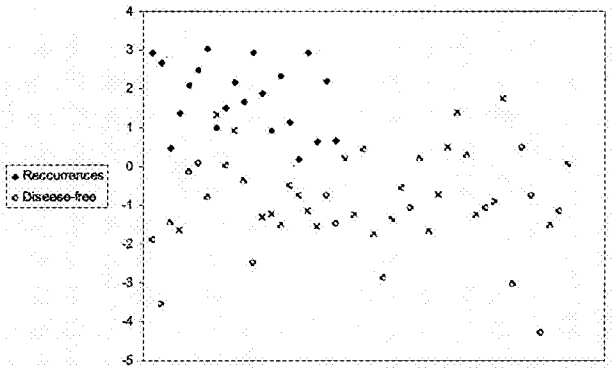

Figure 1: Plot of the discriminant function of all patients showing a very good discrimination between disease-free patients and patients with recurrent breast cancer.

Group 1 – Nucleotyping
Group 2 – DNA ploidy
CCR – correct classification rate

This study is still ongoing and our early data suggest large scale genomic instability studies may provide an accurate method of prognosticating patients.

O-121. End of 4 node sampling? Comparative morbidy versus sentinel lymph node biopsy in the ALMANAC trial

Monypenny IJ, Dixon JM, Kissin M, Newcombe RG, Goyal A, Mansel RE *on behalf of the ALMANAC Trialists Group*

Background: This randomised trial compares the postoperative morbidity of sentinel lymph node biopsy (SLNB) with four node sampling (FNS) in patients with early stage breast cancer.

Methods: Patients with clinically node-negative invasive breast cancer, planned to undergo four node sampling were randomised to SLNB or four node sampling in this multicentre trial. The primary outcome measure was axillary morbidity. From November 1999 to October 2003, 229 patients were randomized to undergo SLNB (120) or FNS (109). The sentinel lymph node was identified using a combined technique involving Patent Blue V and 99mTc-albumin colloid injected peritumorally. Patients with axillary nodal metastases proceeded to axillary clearance or received axillary radiotherapy (non-randomised). The intention to treat analyses of data to 6 months are presented in this paper.

Results: The failed localisation rate for SLNB was 2%. Axillary metastases were similar in both SLNB and FNS arms (24.2% vs. 16.5%, $p = 0.152$). Sensory loss and lymphedema at 6 months were significantly worse after FNS ($p = 0.005$, $p = 0.021$). Axillary operative time, drain usage, hospital stay and time to resume normal day-to-day activities were similar in the two groups.

Conclusions: Sentinel node biopsy is associated with reduced arm morbidity compared to four node sampling and should now be considered standard of care in early breast cancer.

O-122. Age related quality of life (QoL) benefits: results from the Almanac Trial with 18 months follow-up

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The ALMANAC trial is a UK based multi-centre RCT of patients with clinically node negative breast cancer in which sentinel node biopsy (SNB) is compared with standard axillary surgery (level I-III axillary lymph node dissection or 4 node sampling). Previous reports in the literature regarding the consequences of axillary treatment on QoL in patients of different ages have been inconsistent. In our study 829 patients completed 2 standardised questionnaires; the FACT-B+4 to assess QOL and the STAI to assess anxiety. Questionnaires were given prior to randomisation at baseline and at 1, 3, 6, 12 & 18 months post-surgery. Patients were categorised into 3 age groups-: under 50 years ($n = 154$), 50 to 64 years ($n = 494$) and 65 years and older ($n = 181$). The primary endpoint was the Trial Outcome Index (TOI), a summation of physical and functional well-being and breast cancer concerns, including 5 items on arm functioning. Change in TOI from baseline to each of the follow-ups examined the effects of treatment group (standard or SNB) and age. This revealed a significant main effect of treatment in favour of the SNB group (1 month $p < 0.001$, 3 months $p = 0.027$, 6 months $p = 0.017$, 12 months $p = 0.011$, 18 months $p = 0.006$) and a significant main effect of age in favour of older patients for 6 months post-surgery ($p < 0.001$). Changes in arm functioning from baseline to each follow-up showed a significant main effect of treatment in favour of the SNB group ($p < 0.001$) and a significant main effect of age in favour of older patients ($p < 0.003$). Changes in anxiety throughout he trial were unrelated to treatment group, but there was a significant main effect of age for 6 months post surgery, in favour of older patients (1 month $p < 0.001$, 3 months $p = 0.01$, 6 months $p = 0.007$). The impact of breast cancer diagnosis, primary surgery and adjuvant therapy may also affect QoL differently depending on a patient's age.

O-123. Axillary relapse following axillary surgery

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The aim of this study was to assess axillary recurrence in patients treated by axillary sampling alone (ANS), axillary sampling with radiotherapy (ANS+RT) or axillary clearance (ANC). 1816 patients were treated between 1981 to 1998 by breast conserving surgery plus radiotherapy to the breast. Some patients were randomised in an ANS v ANC trial but generally patients with clinically involved nodes or larger tumours (>2 cm) had ANC, those witlh clinically negative nodes and smaller tumours (≤2 cm) were treated by ANS with radiotherapy to the axilla for all node positive patients except for 18 patients who took part in the Scottish Conservation Trial. These and 4 patients who received radiotherapy after an axillary clearance were excluded from this analysis. The minimum follow up of this group is 5 years. The results are as follows:

	5 yr recurrence	5 yr survival	10 yr survival
Node −ve			
ANC	0.5%	90.5%	86.5%
ANS + RT	1.4% $p = 0.008$	92.9%	88.2%
ANS	2.3%	95.6%	93.0%
Node +ve			
ANC	5.1%	77.8%	67.4%
ANS + RT	8.2% NS	85.5%	71.5%

Although the recurrence rate in node −ve patients is higher after ANS, overall survival is not compromised and in node +ve cases recurrence rates after ANS + RT and ANC are not significantly different suggesting that ANS + RT is an alternative to ANC in these cases. Similar results might be expected with node positive sentinel node biopsy followed by radiotherapy.