

ciated with increased local recurrence rates. Only 30–40% of re-excisions, however, contain further tumour. The aim of this paper was to determine if there are any histological factors which can predict a subgroup of patients with positive surgical margins who do not require re-excisions.

This is a retrospective review of 112 patients requiring re-excision for positive margins, defined as <1 mm margin for invasive cancer or ductal carcinoma in situ (DCIS). Seventy-two patients (64%) had negative re-excisions while 40 (36%) had residual disease on re-excision. The mean age, side of the cancer, number of patients with family history of breast cancer and palpability of the cancers were similar between the 2 groups. There was a higher proportion of patients with lobular subtype and node positive disease in the positive re-excision group as compared to the negative re-excision group.

In this study, only 35% of patients undergoing re-excisions for positive margins had further disease. While there was a higher proportion of patients with lobular subtype in the positive re-excisions group, this was not statistically significant ($p = 0.09$). There was a statistically significant number of patients with node positive disease in the positive re-excisions group ($p = 0.002$). We did not, however, identify a particular factor which would predict for a subgroup of patients who would have negative re-excisions. All positive margins should therefore be re-excised.

O-46. Relationship between presence of lobular carcinoma in situ and risk of local recurrence in patients with primary breast cancer treated with breast conserving surgery and radiotherapy

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In an otherwise benign biopsy, lobular carcinoma in situ (LCIS) has been associated with an increased risk of developing breast carcinoma. However, the association between LCIS and risk of local recurrence (LR) in patients with Breast conserving surgery (BCS) and radiotherapy (RT) is debated.

Of 2800 cases of invasive breast cancer diagnosed and treated in Nottingham between 1996 and 2003, 1.8% ($n = 53$) were identified that had been treated by BCS and RT and had surrounding LCIS. No attempt was made for complete excision of LCIS at the margins in these cases but invasive disease and any surrounding DCIS was at least 5mm clear at the margins. A control cohort ($n = 509$) was selected from the same dataset, which were matched for size, VI and NPI.

Median age was 63.8 years with a median follow up of 32 months. Significant associations were seen only with ER positive disease ($p < 0.005$) and lobular type ($p < 0.005$). There was no relationship with the presence of surrounding LCIS and grade, size or vascular invasion (VI). Local recurrence rate in the LCIS group was 1.9% vs 1.4% in the controls ($p = 0.55$). There were no events of contralateral disease or distant metastasis in the series to date.

BCS and RT is an appropriate form of treatment in tumours with surrounding LCIS. Its presence does not appear to significantly increase the risk of LR.

O-47. Does mastectomy for involved margins confer advantage over further local excision to clear margins following conservative surgery in early breast cancer?

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This study compares early results (36/12) after mastectomy (Group A, $n = 67$) with those achieved after re-excision (Group B, $n = 38$) following incomplete wide local excision for operable breast cancer.

Method: Between 1 January 1996 and December 2001, 430 consecutive patients received wide local excision (WLE) for operable invasive breast cancer. All patients had lymph node sampling or clearance at the initial procedure and patients with involved margins either underwent re-excision (Re-ex) or mastectomy (Mx). Patients with positive nodes received axillary radiotherapy or clearance. Systemic adjuvant treatment and irradiation to the conserved breast or mastectomy flap was prescribed according to local protocols. Local and Regional recurrence and distant metastasis at 36/12 were compared between Group A and Group B.

Results:

Minimum follow up (FU) = 36/12 and median follow up = 6 years

Final Operation	WLE	Re-ex	Mx
Total number of patients	325	38	67
Patients lost for Follow up	15	2	3
Patients deceased during study period	15	2	6
LR 36/12	3	1	1
No LR 36/12	293	33	57
RR 36/12	8	1	4
No RR 36/12	290	33	54
DM 36/12	9	1	4
No DM 36/12	291	34	56

LR = Local Recurrence RR = Regional recurrence DM = Distant Metastasis. All figures relate to absolute numbers at 36/12 follow up.

Conclusion: There is no early advantage of completion mastectomy over re-excision after inadequate wide local excision for primary breast cancer.

O-48. Timing of radiotherapy and survival in breast-conserving therapy

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Purpose: To estimate the effect of delay in timing of radiotherapy in breast-conserving therapy (BCT) on local recurrence and distant metastasis.

Methods and materials: We analysed our prospective cohort of 1391 BCT, stage I or II, node-negative breast cancer patients without adjuvant systemic therapy. Seven hundred and thirty patients started the radiotherapy in the same month or one month after lumpectomy (<2 months), 546 in the second month (=2 month), and 115 started radiotherapy in the third month (=3 month). Median follow-UR was 88 months.

Results: There was no difference in local relapse-free survival (LRFS) between the three groups, the 7-year LRFS rates were respectively, 95.6% for <2 months, versus 97.0% for =2 months, versus 97.7% for =3 months. The 7-year distant metastasis-free survival (DMFS) was 85.1% for <2 months,

versus 92.0% (HR 0.5; $p = 0.001$) for = 2 months, versus 96.1% (HR 0.3; $p = 0.029$) for = 3 months. In multivariate Cox regression analysis timing = 2 months was significantly related to an increased DMFS (HR 0.6). The 7-year disease-free survival was 82.3% for <2 months, versus 89.1% (HR 0.6; $p = 0.001$) for = 2 months, versus 90.2% (HR 0.5; $p = 0.066$) for = 3 months. The 7-year disease specific survival (DSS) was 89.3% for <2 months, versus 94.4% (HR 0.5; $p = 0.009$) for = 2 months, versus 97.1% (HR 0.4; $p = 0.148$) for = 3 months. Also in multivariate Cox regression analysis timing = 2 months was significantly related to an increased DSS.

Conclusion: Starting the radiotherapy in the second month or even the third month after lumpectomy seems to have a beneficial effect on distant metastasis and survival, and no effect on local control.

O-49. Accuracy of intraoperative radiology in assessing tumour proximity to resection margins during breast conserving surgery

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The role of intraoperative radiology of the excised specimen during breast conserving surgery remains controversial. The aim of this study was to assess sensitivity, specificity and interobserver variation in close margin assessment using intraoperative radiology.

Radiological margins of 5, 10, 15 and 20 mm were compared to definitive histology in 116 consecutive patients. Sensitivity and specificity were calculated for each radiological measurement for the superior, inferior, lateral and medial specimen margins. Receiver-operator curves were plotted to determine the optimum area under the curve (AUC). A second observer measured margins in 43 patients, to assess interobserver variation.

A radiological standard of 15 mm maximised AUC for the inferior and lateral margins: AUC 0.81, 95% confidence interval (CI) 0.70–0.92, and AUC: 0.611, 95% CI 0.29–0.94 respectively. For the superior margin, using a 10 mm standard maximised the AUC: 0.725, 95% CI 0.52–0.97. For the medial margin, a 5 mm standard maximised the AUC: 0.79, 95% CI 0.60–0.98. Interobserver Kappa score for assessing close superior and inferior margins were 0.82 and 0.59 (indicating excellent and good agreement, respectively).

Different radiological margin measurements should be used for each margin to maximise the specificity and sensitivity of Intraoperative radiology during breast conserving surgery.

O-50. The expression of apoptosis-regulating proteins in usual ductal hyperplasia with known outcome

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Members of the bcl-2 family are key regulators of apoptosis. Bcl-2 blocks apoptosis whereas Bax promotes apoptotic cell death. Their precise role in mammary carcinogenesis remains poorly understood. The relative expression of bcl-2 and bax

would define the phenotypic behaviour of mammary epithelial cells. A case-control study was designed on 674 benign breast specimens received in three institutions in the period between 1979 and 1999. Study cases included all patients with benign breast lesions followed by in situ or invasive cancer of either breast at least 6 months after the benign lesion. Each study case was age and date of biopsy matched with three controls that had histories of benign breast lesions but did not develop breast cancer. Foci of hyperplasia of usual type (HUT) and adjacent morphologically normal lobules were identified from cases and controls and stained with monoclonal antibodies for bcl-2 and Bax. The results were correlated with ER α , ER β and Ki67 expression. The median percentage of bcl-2 expression in HUT foci from patients who progressed to breast carcinoma was 50 whereas that of controls was 17.5, $P < 0.001$. A trend towards higher bcl-2 expression in normal lobules from patient who progressed to breast cancer was seen. Bax was highly expressed in normal lobules from controls when compared with cases ($P = 0.008$). HUT foci from cases exhibited significantly higher content of ER α , ER α /ER β ratio and Ki67 when compared with controls. Using multiple logistic regression analysis, the correct classification rate of bcl-2 and Bax in classifying cases and controls was 70.2%. Our data show, for the first time, an early dysregulation of the levels of apoptosis-regulating proteins in normal and non-atypical hyperplastic foci of patients who progressed to breast cancer.

O-51. Cox-2 inhibition increases apoptosis in human ductal carcinoma in situ (DCIS) of the breast in a xenograft model

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Cyclooxygenase-2 (COX-2) expression is a poor prognostic factor in invasive breast cancer and DCIS. To determine the effect of COX-2 inhibition on human DCIS we compared the effect of Celecoxib (a COX-2 inhibitor) with placebo, in a nude mouse xenograft model, using DCIS samples collected from women undergoing mastectomy (after ethical approval and informed consent). The DCIS was dissected into 1x2x2mm sections and eight sections were implanted subcutaneously into female nude mice. After 14 days, two DCIS xenografts were harvested and treatment was started with either 0.15% Celecoxib or control. Following 14 days of treatment, the remaining xenografts were harvested. The DCIS was assessed by immunohistochemistry for Ki67 (a marker of cell proliferation), apoptosis (H&E morphology) and COX-2 protein expression.

Celecoxib treatment decreased COX-2 expression ($p = 0.0001$; see table) and increased apoptosis ($p = 0.005$). No changes in cell proliferation were seen.

Day	Ki67 (%)		Apoptosis (%)		COX-2 (%)	
	14	28	14	28	14	28
Median Control	5.5	2.7	1.5	1.7	42.3	43.4
[IQR]	[2.9–9.0]	[1.6–5.8]	[0.9–2.7]	[0.8–3.0]	[35.8–56.7]	[34.8–48.2]
Median Treated	4.7	4.3	1.4	2.4	45.3	26.3
[IQR]	[1.9–6.8]	[2.0–7.5]	[1.0–1.7]	[1.3–3.7]	[32.3–58.2]	[16.3–39.2]
P value	0.5		0.005		0.0001	

[IQR] = Interquartile range