

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