Celecoxib significantly decreases COX-2 protein expression and increases the rate of apoptosis in human DCIS and is a promising adjuvant therapeutic strategy for Ductal Carcinoma In Situ.

O-52. Activated c-Src in ductal carcinoma in situ correlates with high grade and HER2 expression

Wilson G, Barnes N, Knox F, Swindell R, Kawakatsu H, Dive C, Bundred N. *University Hospital of S Manchester & University of California USA*

Background: The non receptor tyrosine kinase c-Src is downstream of HER2 and activation of c-Src influences response to Herceptin, and tumour progression and metastasis.

Aim: To determine the expression of activated c-Src in pure DCIS and determine if activated c-Src correlates with HER2 expression and clinicopathological parameters in DCIS.

Method: Immunohistochemical expression of activated c-Src using Clone 28 monoclonal antibody was evaluated in 78 patients (median age 55 years, range 39–71 years) with "pure" DCIS and a median follow-up of 60 months (range 24–240). HER2, HER4, ER and Ki67 levels were evaluated by immunohistochemistry. A HER2/HER4 score ≥ 2 was considered positive.

Results: Forty-three (out of forty-seven) HER2 positive tumours expressed active c-Src ($p < 0.015$). Strong expression of activated c-Src was also associated with high tumour grade ($p < 0.0005$) in 78 DCIS examined, but not epithelial proliferation (measured by Ki67, $p = 0.450$), tumour size, ER status and HER4 expression.

Characteristic		% DCIS Activated c-Src	P value
HER2	score ≥ 2	91% (43/47)	0.015
HER4	score ≥ 2	88% (22/25)	0.549
ER	positive	67.6% (52/77)	0.499
Tumour grade			
Low		10.3% (8)	
Intermediate		32% (25)	
High		57.7% (45)	$P < 0.0005$

Conclusion: Activation of c-Src is seen in high grade DCIS lesions with HER2 expression. Interruption of c-Src signalling with small molecule inhibitors may be therapeutically useful.

O-53. Accuracy of mammography in predicting histological extent of DCIS

Chakrabarti J, Evans AJ, James J, Pinder SE, Ellis IO, Macmillan RD. *Nottingham City Hospital*

Mammographic (MMG) extent is the main determinant for offering wide local excision for DCIS. It is recognized that this does not always correlate accurately with histological (HIST) extent. The aim of this study was to define the degree of variance between MMG and HIST measurement of DCIS and analyze the factors predicting a significant discrepancy.

The HIST and MMG data for 174 cases of DCIS were reviewed. The MMG size was bigger than the HIST size in 97(55.7%) and there was >10 mm difference in 18 (10.3%) of cases. The HIST size was bigger than the MMG size in 69 (39.7%) of cases and >10 mm difference in 30(17.2%) of cases.

The association between a variance in MMG/HIST extent and various factors is shown in the table below.

	MMG > HIST		HIST > MMG	
	>10 mm	1–10 mm	1–10 mm	>10 mm
Mean MMG size in (mm)	26.6	14.6	12.6	19.1
% High Grade	61.1	59.5	66.7	70.0
% Dense MMG	5.9	15.6	18.4	13.3
% Involved Margins	16.7	17.9	23.7	80

The only statistically significant finding was that cases with a HIST > MMG variance >10 mm were more likely to require further surgery for involved margins. We were unable to find factors that pre-operatively identified these women.

The important findings of this study are that MMG undersizes DCIS in over a third of cases and there is no reliable method for identifying this group. Other methods of pre-operative imaging should be explored.

O-54. Factors predicting recurrence in DCIS after breast conserving surgery with clear margins

Wilson G, Remouche S, Barns N, Knox F, Swindell R, Bundred N. *University Hospital of S Manchester*

Background: Factors predicting recurrence following breast conserving surgery (BCS) with clear margins for Ductal Carcinoma In Situ (DCIS) are largely unknown.

Aim: To determine recurrence rates and predictors of recurrence risk in patients who underwent BCS with clear margins (>1 mm) for pure DCIS.

Method: We reviewed all patients who underwent BCS ($n = 305$) for pure DCIS and then excluded patients with involved margins ($n = 76$) to determine what factors predicted recurrence in patients with clear margins ($n = 229$). ER, HER2, and Ki67 were measured by immunohistochemistry. A HER2 score ≥ 2 was considered positive.

Results: Margin status was a highly significant recurrence predictor ($p \leq 0.001$). Overall recurrence was 13.1% (30/229) in patients with clear margins at 5 years and 31.6% (24/76) with involved margins. In the group of women with clear margins after BCS ($n = 229$), high epithelial proliferation (measured by Ki67, $p = 0.044$) and HER2 positivity ($p = 0.042$) were associated with increased recurrence. 75% of recurrent DCIS had a Ki67 $\geq 10\%$ compared to 50% in the non-recurrent group 39% of HER2 positive DCIS recurred at 5 years compared to 16% HER2 negative. Tumour grade, size and age at diagnosis did not predict recurrence.

Patient Characteristics BCS + clear margins		Non-recurrent $n = 199$	Recurrent $n = 30$	p value (Log Rank)
HER2 positive (% ≥ 2)		44	70	0.042
Ki67	Median	10.1	13.2	
	Range	0.8–38	2.5–38.8	0.044
ER positive %		77.6	61.5	0.316
Tumour Grade	Low	16	1	
	Intermediate	47	8	
	High	118	21	0.496