of clinical, pathological and treatment characteristics were evaluated with respect to risk on recurrence.

Methods and Materials: Four hundred and three (403) cases of DCIS underwent surgery at the Netherlands Cancer Institute/Antoni van Leeuwenhoek hospital (NKI/AvL) from January 1986 to December 2002. All patients with 'pure' DCIS and no prior history of breast cancer were included.

The clinical and pathological characteristics evaluated were: age, detection method, biopsy method, number of surgical procedures, completeness of excision and histological grade.

The main endpoints of this study were local recurrence, either invasive or non-invasive, metastasis, and breast cancer-specific mortality.

Results: One hundred and sixty five patients (41%) were treated with breast-conserving therapy, 97 (24%) with excision alone, and 68 (17%) with excision plus radiotherapy, and 238 (59%) with mastectomy. Median age was 51.0 years (range: 24–81 years).

At a median follow-up of 5.3 years, 20 events occurred. Eight patients (8.2%) had local recurrence in the excision alone group, 7 patients (10.3%) in the excision plus radiotherapy group and 5 patients (2.1%) in the mastectomy group (4 local and 1 distant). Median time to recurrence was 2.9 years for all groups. Four (1%) patients died of invasive breast carcinoma after recurrence after a mean follow-up of 4.4 years.

Histological differentiation grade of primary tumour and margin status are not equally distributed. The poorly differentiated and margin positive tumours are more present in the excision plus radiotherapy group than in the excision alone or mastectomy group, 62/25% vs. 27/18%, and 51/4% respectively.

Contralateral breast cancer developed in 7 (7.2%), 2 (2.9%) and 12 (5%) cases in the excision alone, excision plus radiotherapy and mastectomy group respectively.

Conclusion: Breast cancer relapse rates in this series are according to generally accepted standards. The differences in risk factors between the three treatment modalities may reflect physician preferences, resulting in a relatively large proportion of patients treated with mastectomy (with either simple or skin-sparing reconstruction).

461 ORAL

Outcome after invasive recurrence in patients with ductal carcinoma in situ of the breast

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Objective: Local recurrence (both invasive and non-invasive) has always been used as the most important marker of treatment failure for patients with ductal carcinoma in situ (DCIS). As follow-up lengthens, additional endpoints become increasingly important. Chief among these endpoints are distant recurrence and breast cancer specific fatality caused by invasive recurrence.

Methods: A prospective database was used to analyze 1136 nonrandomized patients treated for DCIS. Endpoints included invasive and non-invasive local recurrence, distant recurrence, breast cancer specific fatality and overall fatality. All recurrence and fatality data were 10 year actuarial (Kaplan-Meier).

	Excision + Radiation	Excision Only	Mastectomy
Number of Patients (n=1136)	286	444	406
Total Recurrences (n=129)	51	73	5
Invasive Recurrences (n=57)	26	27	4
Distant Metastases (n=11)	7	2	2
Breast Cancer deaths (n=8)	6	2	0
Average DCIS Size	19 mm	16 mm	43 mm
10-Yr Local Recurrence Rate	18%	30%	1.8%
10-Yr Distant Recurrence Rate	2%	1.2%	1%
10-Yr Breast Cancer Specific Fatality	2%	0.7%	0%
10-Yr Overall Fatality (all causes)	8%	8%	9%

Conclusions: These results indicate that most patients with DCIS who recur can be salvaged, regardless of their initial treatment. For the small subgroup of patients who recur with invasive breast cancer, mortality rate is similar to patients with T1a or T1b node negative (Stage 1) primary breast cancer.

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Ductal carcinoma in situ (DCIS) in elderly women. Results according to treatment

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Background: To evaluate the outcome in elderly women with DCIS treated in current clinical practice.

Material and Methods: From January 1985 to December 1996, 1223 women with pure DCIS were treated in 9 French Cancer Centers, by mastectomy (M): 358 (29%), conservative surgery alone (CS): 265 (22%) or conservative surgery with radiotherapy (CS+RT): 600 (49%). 76 (6.2%) women were 70 years old or more (70–75 y: 52; 76–80 y: 17; >80 y: 7), with a 73.3-year median age. The median follow-up for this group was 74.8 months (versus 94 months for the entire cohort). These patients were treated by M: 26 (34%), CS: 18 (24%) and CS+RT: 32 (42%). A family history of breast cancer (BC) was reported in 28% of the cases, and 54% of the lesions were discovered by mammography. 27 out of 76 (35%) lesions were comedocarcinoma subtype.

Results: the 6-year local recurrence (LR) rates were 3.8% (1/26), 22% (4/18) and 0% (0/32) in M, CS and CS+RT groups, respectively (p=NS). Three were in situ LR and two were invasive. No nodal recurrences were observed. Only one woman developed metastases after an invasive LR. Five women developed a contralateral BC and two a second cancer.

Conclusion: Clinical and histological features of DCIS in elderly women are quite similar to those observed in younger women, as well as treatment modalities distribution. CS+RT leads to a particularly excellent local control in elderly patients, as well for DCIS as for infiltrating carcinoma.

463 ORAL

Ductal carcinoma in situ (DCIS) – the role of prognostic indicators in informing treatment and reducing local recurrence

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The incidence of Ductal Carcinoma *In Situ* (DCIS) has risen dramatically in the West Midlands since the introduction of the National Health Service Breast Screening Programme (NHSBSP). There is a wide variation in treatment provided to these patients and uncertainty as to the best management policy to follow.

840 cases of DCIS diagnosed during the period 1st April 1988 – 31st March 1999 were identified in 10 breast screening services in the West Midlands. Treatment and follow-up data were collected from hospital case notes and from the West Midlands Cancer Intelligence Unit's cancer registration database. A pathological slide review was undertaken by a consultant pathologist to provide consistent information on diagnostic characteristics. A radiology review of the diagnostic X-ray films was undertaken to gain information on particular radiological characteristics of these patients. 624 cases were identified with a full pathology dataset and 718 cases with a full treatment dataset. The 586 cases with both a full pathology and treatment dataset were then subjected to radiological review. After further exclusions, cases with a full radiology, pathology and treatment dataset were then analysed. Follow-up data were attained for a maximum of 14 years and a minimum of 3 years.

Data will be presented which link the radiological characteristics, pathological findings, treatment methodologies undertaken and resultant outcomes in terms of time to local recurrence. There were 72 recurrences overall of which 54 were local (ipsilateral or bilateral) giving a local recurrence rate of 9.22%. Mean time to local recurrence was 35.65 months and this figure differed depending on margin status, surgical procedure, and

whether radiotherapy was given. The local recurrences were predominantly non-invasive and came from high grade original primaries. Hypotheses will be developed to suggest associations between radiological characteristics and the likely pathological findings and the prognostic significances of these identifiers.

464 ORAL

Micrometastases in sentinel lymph nodes of patients with ductal carcinoma in situ of the breast should have no consequences for further treatment

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Background: (Micro-)metastases may be detected in sentinel axillary lymph nodes of patients with in situ carcinoma of the breast or small invasive carcinomas. For some surgeons this is a reason to routinely perform a sentinel node procedure in situations otherwise known to have an excellent prognosis without axillary staging. The incidence and predictive value of these positive nodes is uncertain.

Methods: The authors used cases from the Netherlands Cancer Institute to determine the incidence of lymph node metastases in ductal carcinoma in situ (DCIS) and small invasive carcinoma after immunostaining. All consecutive patients with primary breast cancer were selected that were treated between 1989 and 1998 and had undergone axillary dissection as part of their treatment. Patients were identified with pure DCIS (n=71), DCIS with microinvasion (n=12), invasive ductal/lobular carcinoma (IDC/ILC) ⩽5 mm (n=18) or tubular carcinoma ⩽10 mm (n=17). All archived lymph nodes of these patients were re-evaluated using immunohistochemistry (IHC) at deeper levels.

Results: More metastases were found with the use of IHC. In DCIS the incidence increased from 1.4% with routine staining to 11% with IHC. For DCIS with microinvasion <2 mm it was 0% versus 27% respectively. In IDC/ILC sized 2–5 mm the incidence rose from 6% to 12% and in tubular carcinoma ⩽10 mm from 0% to 12%. All but one of the immunohistochemically detected metastases were solitary cells (n=9) or micrometastases (n=4). Maximally two nodes per patient were affected. None of the patients with positive lymph nodes died during follow-up (mean 102 months).

Conclusions: Because 1) micrometastases do not have the same prognostic significance as macrometastases and 2) survival of our patients does not appear to be influenced by micrometastases, we advise not to perform an ALND when a micrometastasis is found in the sentinel node of a Tis or T1a tumor.

465 POSTER

Predicting recurrence risk in DCIS: The role of Type 1 tyrosine kinase receptor co-expression

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Background: Up to 20% of patients with DCIS recur following breast-conserving surgery and radiotherapy, half of which are invasive. The type 1 tyrosine kinase receptor HER2(c-erb2/neu) is associated with resistance to hormone therapy and early recurrence in invasive breast tumours. Determining the patterns of co-expression of HER2 with another type 1 tyrosine kinase receptor – HER4 and other tumour markers may aid prediction of recurrence risk following surgery for DCIS. We studied 135 women with DCIS (follow up: range 3–12 years, median 5 years), 42 patients who had recurred (29 recurrent DCIS and 13 invasive disease,) and 94 patients who had not recurred.

Methods: The primary DCIS of the cases were compared for HER2, HER4, oestrogen receptor (ER), cyclooxygenase-2 (COX-2) and Ki67 antigen (a marker of proliferation) expression by immunohistochemistry. HER2/4 and COX-2 were scored 0 (absent) to 3 (maximum). Scores ⩾2 were taken as over-expression. ER was scored positive if ⩾5% of cells stained. Ki67 antigen was expressed as the percentage of positively staining cells. At least 1000 cells were counted for each section.

Results: Of the non-recurrent lesions 57% were HER2 positive and 63% HER4 positive, compared to 81% HER2 positive (p=0.007*) and 40% HER4 positive (p=0.003*) in the recurrent group. Co-expression of HER2 with HER4 was associated with a reduced recurrence compared to HER2 positive tumours that lacked HER4 (p=0.003*). This association remained significant when stratifying for both high-grade (p=0.015*) and breast-conserving surgery (p=0.0001*). HER4 positive DCIS was more likely to be ER positive than HER2 positive DCIS (74% vs. 51%) p=0.048*. ER status did not influence recurrence in HER4 positive tumours (p=0.8*). None of the HER4 positive/HER2 negative recurrences were invasive. HER2 positivity was associated with a higher and HER4 positivity a lower percentage of proliferating cells (mean 19.3 vs. 10.4%) (p=0.004**). 70% of the non-recurrent cases were COX-2 positive compared with 87% of the recurrent cases (p=0.039). There was no relationship between COX-2 and either HER2/4 co-expression or ER status.

	Receptor Co-expression					
	HER2neg/ HER4neg	HER2pos/ HER4neg	HER2neg/ HER4pos	HER2pos/ HER4pos	Total	p value
N=No recurrence (%)	11 (12%)	23 (25%)	29 (31%)	30 (32%)	93	p=0.008*
N=Recurred (%)	5 (12%)	20 (48%)	3(7%)	14 (33%)	42	
Mean Ki67 (%)	13.4	19.3	10.6	15.4		p=0.004**

*Chi-square, **Kruskal-Wallis test.

Conclusion: Co-expression of HER4 with HER2 reduces the risk of early recurrence of DCIS compared to HER2 over-expressing tumours lacking HER4. COX-2 negativity is also associated with a lower risk of recurrence. The assessment of type 1 tyrosine kinase receptor co-expression and COX-2 expression can aid the prediction of recurrence risk in DCIS.

466 POSTER

Trends in diagnosis and treatment of ductal carcinoma *in situ* of the breast in 403 cases over 1986–2002

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Background: The aim of this study is to watch the trends in diagnosis and treatment of 403 cases of ductal carcinoma *in situ* (DCIS) over the period 1986–2002. The impact of clinical, pathological and treatment characteristics were evaluated with respect to risk on recurrence.

Methods and Materials: Four hundred and three (403) cases of DCIS underwent surgery at the Netherlands Cancer Institute/Antoni van Leeuwenhoek hospital (NKI/AvL) from January 1986 to December 2002. All patients with 'pure' DCIS and no prior history of breast cancer were included.

The clinical and pathological characteristics evaluated were: age, detection method, biopsy method, number of surgical procedures, completeness of excision and histological grade.

Mainly, the effect of the introduction of mammographic screening and stereotactic core biopsy on treatment policy was studied.

Results: One hundred and sixty-five patients (41%) were treated with breast-conserving therapy, 97 (24%) with excision alone, and 68 (17%) with excision plus radiotherapy, and 238 (59%) with mastectomy. Median age was 51.0 years (range: 24–81 years).

DCIS detected mammographically increased from 50% in the late eighties to 83.6% in the nineties, whereas the number of symptomatic lesions decreased from 28.9% to 14.8%. Since the introduction 10 years ago, more than 70% of all DCIS are diagnosed by stereotactic core biopsy now. As a result, the number of surgical multi-step procedures necessary for definite treatment declined from 76.5% in 1995–1997 to 41% in 2001–2002. Today, 59% of DCIS patients are being treated surgically in one step.

The breast-conserving therapy/mastectomy ratio did not change over time with about 60% of patients treated ultimately by mastectomy (with either simple or skin-sparing reconstruction).

Conclusion: This study shows an increase in mammographically detected DCIS and in the use of stereotactic core biopsy in diagnosing DCIS over the last decade. The latter caused a decline in multi-step surgical procedures and in the number of positive margins after first surgery. The introduction of mammographic screening did not reduce the rate of mastectomies.

467 POSTER

Lobular carcinoma in situ – correlation of grading with invasive carcinoma and with ductal carcinoma in situ

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The aim of the study was to assess the value of some histopathological parameters in evaluating lobular carcinoma in situ as a risk factor for the development of ipsilateral and contralateral ductal or lobular