these cases underwent a mastectomy; whereas the overall mastectomy rate was 50%.
Analysis of the cases collated by the BCCOM project in years 1–3 will be undertaken to evaluate data quality and performance. Delegates at the conference will be invited to comment on the measures developed, and the use of these measures as possible surrogates for patients' clinical outcomes will be discussed.

O-7 Micro-RNA expression profiling in primary breast tumours

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Introduction: The role of micro-RNAs in the regulation of proliferation, differentiation and apopotosis has advocated them as a novel molecular mechanism in the aetiology of carcinogenesis. MicroRNA expression has been shown to be dysregulated in a number of human cancers, including breast cancer.
Aims: To identify microRNAs that are abberantly expressed in breast tumour tissue and examine correlations with established clinicopathological variables.
Methods: Whole genome microRNA profiling was performed in six early stage breast cancer specimens. Expression of selected differentially expressed microRNAs was validated using RQ-PCR in a larger cohort of 54 breast tumours, 5 benign, and 5 normal breast tissues. Associations between relative expression of specific microRNAs, established clinicopathological variables and hormone receptor status were examined.
Results: 53 of 452 microRNAs were differentially expressed across the six tumour samples. Specific microRNAs which were validated in the larger cohort of samples using RT-Q-PCR included *miR-21, miR-195, miR-10b* and *miR-154**. Tumour samples exhibited higher *miR-21* expression than normal breast tissue. Conversely, *miR-10b* and *miR-195* were consistently expressed at lower levels in tumour versus benign and normal breast tissue. *MiR-195* and *miR-154** expression was significantly lower in oestrogen receptor positive *(ER)* than *ER* negative tumours. ($p = 0.005$, $p = 0.001$). Expression was independent of other cliniopathological variables.
Conclusions: The increased expression of *miR21* and decreased expression of *miR-10b* and *miR-195* in tumor tissues implicates these miRNAs in oncogenesis and tumour suppression respectively. We have shown that *miR-195* and *miR-154** are differentially expressed in breast tumours according to *ER* status, highlighting their importance in specific breast cancer phenotypes.

O-8 Factors predicting survival after neoadjuvant therapy with aromatase inhibitors

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Background: Few studies have investigated factors predicting outcome following neoadjuvant endocrine therapy. This study aimed to determine factors predicting survival after neoadjuvant treatment with aromatase inhibitors (AI's).
Methods: 153 postmenopausal women with large/locally advanced estrogen receptor rich tumours (ER 5–8) were treated for 3 months with letrozole, anastrozole or, exemestane. The mean patient age was 74.7 years. Tumour biopsies were obtained prior to starting therapy and at 3 months. At 3 months patients underwent surgery with nodal assessment or, continued AI therapy. Responding patients continued AI therapy post-operatively. Median follow up was 41 months. Five year survival was 63.1% and cause specific survival (CSS) 79.8%.
Results: At 3 months only 3% had progressive disease and 67 had responded (>50% reduction in volume). In the univariate analysis T stage ($p = 0.03$), surgical node status ($p = 0.0005$), Ki67 at diagnosis ($p = 0.036$), 3 month % reduction in Ki67 ($p = 0.0027$) and 3 month Ki67 ($p = 0.03$) were significantly correlated with CSS. In the proportional hazards analysis significant variables were number of positive nodes ($p = 0.0007$), % reduction in Ki67 ($p = 0.0029$) and, tumour grade ($p = 0.0383$). Excluding those available at diagnosis significant variables were baseline Ki67 ($p = 0.02$) and T stage ($p = 0.02$).
Conclusion: In post-menopausal women treated with neoadjuvant AI therapy: (i) Two thirds with ER rich large/locally advanced breast cancers responded to 3 months of treatment and, (ii) Surgical node status, % reduction in Ki67 and, tumour grade predicted death from breast cancer.

O-9 ONCOPOOL – A European Database in 16,893 cases of breast cancer: comparison with SEER

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11 European Breast Units from 10 countries retrospectively entered consecutive cases diagnosed in each unit in periods between 1990–99. Cases were women, age $\leqslant 70$ with primary tumours <5 cm diameter. Data on diagnosis, surgical and adjuvant treatments, pathology and biology, recurrences and survival.

- Factors at diagnosis
  - Tumour size: 21% $\leqslant$1 cm, 28% $\leqslant$2, 29% $\leqslant$3, 10% $\leqslant$4.9
  - LN status: LN neg 66%, LN 1–3+ 24%, LN 3+ 10%
  - Grade: I 29%, II 42%, III 29%
- Second order polynomial curves demonstrate the relations of the three LN stages with tumour size and between grade and stage
- Overall survival was 91% 5 yr, 81% 10 yr and 78% 14 yr (Life table)
- The survival data provides validation of the updated prognosis according to the Nottingham Prognostic Index (to be separately presented).

The US SEER (Surveillance, Epidemiology and End Results) Database has long been regarded as giving the standards in Primary Breast Cancer for distribution of pathological factors and prognoses. There was a great amount of incomplete data.
Comparison of the SEER estimates of prognosis according to TNM are shown in ONCOPOOL to be greatly inferior to other means of estimation (Table).

	TNM	NPI Predicted			ONCOPOOL
	Predicted 10 yr % OS	Grade	NPI Group	10 yr % BCS	Observed 10 yr % BCS
$\leqslant$2 cm, LN –	94	I	EPG	96	94
$\leqslant$2 cm, LN –	94	III	MPG I	81	94
$\leqslant$2.5 cm, LN –	88	I	GPG I	93	93
$\leqslant$2.5 cm, LN –	88	III	MPG II	74	76
$\leqslant$2.5 cm, LN –	76	I	MPG I	81	84
$\leqslant$2 cm, LN –	76	III	PPG	55	53
$\leqslant$2 cm, LN –	58	I	MPG II	74	76
$\leqslant$2.5 cm, LN –	58	III	PPG	55	53

ONCOPOOL is up to date, based on data direct from Units rather than from tumour registries, data is much more complete than SEER, there is greater accuracy in survival prediction and 10 yr survival figures rather than 5 yr are given.
ONCOPOOL should be regarded as the standard European dataset for primary breast cancer.

O-10 Changing pattern of the detection of loco-regional relapse in breast cancer: The Edinburgh Experience

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Guidelines exist for follow-up of breast cancer patients. Follow-up is concentrated on the first three to five years, with either reduced frequency of visits or discharge after this. Guidelines recommend mammography; no evidence exists to inform frequency. We analyse treatable relapses in our unit from 1312 patients with early stage breast cancer treated by breast conserving surgery (BCS) and post-operative radiotherapy between 1991 and 1998 to assess appropriateness of the guidelines. 110 treatable relapses were analysed. Treatable relapse developed at 1–1.5% per year throughout follow-up. 48 relapses were in ipsilateral breast, 25 ipsilateral axilla, 35 contralateral breast and 2 both breasts simultaneously. 37 relapses (33.5%) were symptomatic, 56 (51%) mammographically detected, 15 (13.5%) clinically detected, 2 (2%) diagnosed incidentally. Mammography detected 5.37 relapses per 1000 mammograms. Patients with symptomatic or mammographically detected ipsilateral breast relapse had significantly longer survival from original diagnosis ($p = 0.0002$) and from recurrence ($p = 0.0014$) compared with clinically detected relapse. Treatable relapse occurs at a constant rate to at least ten years. Clinical examination detects a minority (13.5%). Relapse diagnosed clinically is associated with poorer outcome. Long-term follow-up based on regular mammography is warranted for all patients treated by BCS.

O-11 Radiotherapy and/or tamoxifen after conserving surgery for breast cancers of excellent prognosis: BASO II TRIAL

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The BASO II trial was of intact breast irradiation (RT) versus No RT and/or Tamoxifen versus No Tamoxifen following breast conserving surgery, in patients with primary invasive breast cancers of excellent prognosis.
Primary objective: To determine the rates of local recurrence (LR) for the various regimes, defined as further cancer in the tissue or skin of the treated breast.
Secondary objectives: breast cancer specific survival rates; contralateral breast cancer rates.
Method: 2×2 design with entry allowed to one or other comparison as well as to both. Life table analysis (Log Rank) according to randomisation and to treatment received.
Results: Median FU 122 months. 10 year breast cancer specific survival (Life table) 96%.
The results of the randomisation (intention to treat) show that operative surgery without an additional treatment is significantly worse in terms of LR than treatment with either therapy and particularly so when treatment excluded both therapies. There was no significant difference in LR between the addition of RT alone and the use of Tamoxifen alone
Analysis by treatment received (Table) showed the average rate of local recurrence to 10 years of follow-up is 1.6% per annum in the group receiving neither therapy against 0.1% per annum in those receiving both; recurrence rates are 0.5% per annum in those receiving only Tamoxifen and only RT.

Treatment received	No LR n	LR n	LR%	LR rate p.a (%)
No RT no TAM	146	29	16.6	1.6
RT no TAM	172	10	5.5	0.5
TAM no RT	401	20	4.8	0.5
RT + TAM	376	4	1.1	0.1

Conclusions: Even in this group of early tumours of least aggression, wide local excision alone has a rate of LR around 1.5% PA. This rate is significantly reduced by receipt of either RT or Tamoxifen. Recurrence rate is very low at around 0.1% PA following receipt of both adjuvant therapies.

O-12 Radiation therapy after breast-conserving surgery: randomised trial in patients with low risk of recurrence

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To study the role of radiotherapy and Tamoxifen after breast-conserving surgery (BCS) in patients with a favourable prognosis, a clinical trial was initiated by the German Breast Cancer Study Group. Between 1991 and 1998, 361 patients (pT1pN0M0, aged 45 – 75 years, receptor positive, grade I-II) were randomised to radiotherapy (yes/no) and Tamoxifen for 2 years (yes/no) in a 2×2 factorial design; the exclusion of seven centres (14 patients) left 347patients in the analysis.
After a median follow-up of 5.9 years, 77 events concerning event-free survival were observed. Mainly due to local recurrences, the event rate was about three times higher in the group with BCS only than in the other three groups. No difference could be established between the four treatments groups for distant disease-free survival rates. It was concluded that even in patients with a favourable prognosis, the avoidance of radiotherapy and Tamoxifen after BCS increased the rate of local recurrences substantially.
The results of a median follow-up of nine years will be presented.

O-13 Differential expression of ER and Ki67 in normal breast tissue and proliferating breast disease: further support of the progenitor cell concept?

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In 2002/2003 we proposed a progenitor cell model of normal human breast epithelium, in which Ck5/14-positive cells give rise to both the glandular (Ck8/18+) and myoepithelial cell lineages. We further suggested a model of how proliferative lesions and carcinoma develop.
Aim: To test these hypotheses in resting breast epithelium (n = 6), usual ductal hyperplasia (UDH) (n = 4), FEA (n = 3), ADH (n = 6), DCIS (n = 6) and LN (n = 4) using an in-situ double immunostaining method (for example ER vs. Ck8/18, ER vs. Ck5/6, ER vs. ki67, ki67 vs. Ck8/18