between erbB3 and IRS-1 in MCF-7, T47-D and BT-474 cells with HRGβ1 treatment enhancing this recruitment and promoting IRS-1 phosphorylation at tyrosine (Y) 612, a specific PI3-K binding site. In addition, siRNA knockdown of IRS-1 greatly impaired HRGβ1 signalling via PI3-K/AKT in these cells. This novel interaction may have clinical relevance as immunohistochemical analysis of ER-positive BC patient samples revealed IRS-1 Y612 expression positively correlated with total erbB3, p-AKT and Ki67 expression. Importantly, we found that association of IRS-1 by erbB3 impaired IRS-1 recruitment by IGF-IR in both MCF-7 and T47D cells, whilst blockade of IGF-1R enhanced erbB3/IRS-1 interaction and sensitised both cell lines to HRGβ1. Consequently, knockdown of IRS-1 reduced HRGβ1 action and enhanced the effects of IGF-IR inhibition in these cells. In conclusion, these and previous findings suggest that IRS-1 can be recruited to IGF-1R, EGFR and erbB3 in ER-positive BC cells and this may provide an adaptive resistance mechanism when these receptors are targeted individually. Consequently co-targeting of IGF-IR and erbB receptors/IRS-1 may prove to be a more effective strategy for the treatment of ER-positive BC.

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O-37 SOX11 AND PSMD3 EXPRESSION IN HER2 POSITIVE BREAST CANCER

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Human Epidermal Receptor 2 (HER2)+ have attracted attention as a poor prognostic class of breast cancer. However, HER2+ tumours appear to encompass biologically and clinically heterogeneous tumours.

In order to refine HER2+ breast cancer, we analysed over 48,000 gene transcripts in 132 invasive breast carcinomas using Artificial Neural Network analysis and identified high expression of two novel genes (SOX11, PSMD3) significantly associated HER2+ positivity. Using a large invasive breast carcinoma cohort ($n = 1{,}298$), prepared as tissue microarrays, we assessed these targets using immunohistochemistry and investigated associations with clinicopathological variables, patients' outcome and ability to refine HER2+ classification.

PSMD3 nuclear expression was observed in 219/942 (23%) of tumours and was significantly correlated to HER2 positivity ($p = 0.004$), tubule formation ($p = 0.047$) and NPI ($p = 0.007$). PSMD3 expression conferred a strong trend towards a longer breast cancer specific survival in the whole series ($p = 0.065$). SOX11 nuclei staining was observed in 96/869 (3.8%) tumours and was significantly associated with ER ($p = 0.006$) and PSMD3 nuclear ($p < 0.001$) positivity and ck14 negativity ($p = 0.018$) but not HER2. SOX11 expression did not predict patient clinical outcome in either the whole series or HER2+ tumours only.

This study confirms the biological and clinical heterogeneity of HER2+ tumours and the difficulties in translating global gene expression data into routine practice using immunohistochemistry. We have identified two novel genes associated with HER2+ tumours and further studies analysing the role of PSMD3 expression in this important subtype is warranted.

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O-38 DYSREGULATED CANCER-SPECIFIC MiRNAs IN THE CIRCULATION OF BREAST CANCER PATIENTS

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Introduction: Recent seminal findings from our institution indicate that systemic *miR-195* and *Let-7a* levels have potential as non-invasive breast cancer biomarkers. We aimed to validate these findings in an expanded cohort and to identify further miRNAs which augment the sensitivity and specificity of circulating miRNAs as diagnostic and prognostic markers for breast cancer.

Methods: The expression levels of nine miRNAs were evaluated in an expanded cohort of 265 breast cancer patients, 80 non-breast malignancies (colon, renal, prostate and melanoma) and 63 age-matched disease-free controls using RQ-PCR. Eleven additional miRNAs were evaluated as potential miRNA endogenous controls. Advanced QBase plus software and SPSS were used for biostatistical analysis of the data and correlation with clinicopathological variables.

Results: This study confirmed significantly deranged expression levels of systemic *miR-195* and *Let-7a* and two additional miRNAs in breast cancer patients compared to disease-free controls. Elevated *miR-195* was identified to be breast cancer-specific, with a sensitivity of 88% and a specificity of 91%. A combination of three circulating miRNAs, including *miR-195* and *Let-7a*, increased the discriminatory power of this test for breast cancer to 94%. Of the eleven candidate miRNAs selected for normalisation, two were identified to be stably expressed in a subset of the original cohort and thus are ideal endogenous controls for blood based miRNA studies.

Conclusion: This study highlights the presence and dysregulation of cancer-specific miRNAs in the circulation of breast cancer patients and illustrates the potential for this systemic miRNA signature to aid in the diagnosis and prognostication of this disease.

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O-39 HER2 POSITIVE EARLY BREAST CANCERS: WHAT PROPORTION ARE RECEIVING ADJUVANT TRASTUZUMAB THERAPY? A MULTICENTRE AUDIT

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Background: Trastuzumab was licensed for adjuvant therapy in early breast cancer (EBC) in the UK in 2006. The objectives of this multicentre audit were to determine the incidence of HER2+ breast cancers, proportion of HER2+ EBC women who received Trastuzumab and ascertain reasons why some HER2+ patients did not receive Trastuzumab.

Methods: Data collected for all invasive breast cancers diagnosed at seven UK centres over 18-months from 2007 onwards. All HER2+ cancers diagnosed by a combination of IHC and FISH identified using each centre's database. Case records checked and reasons noted if they had not received Trastuzumab.

Results: Patients (4488) diagnosed with invasive breast cancer. 645 (14%) were HER2+ cancers, 523 being EBCs. 326 (62%) HER2+ EBCs received Trastuzumab.

Reasons for not receiving Trastuzumab	*n* = 197(%)
Tumour ⩽10 mm, node negative	65(33)
Small node negative tumours (11–20 mm)	18(9)
Age	42(21)
Comorbidities	27(13)
Therapy refused	28(14)
Other reasons	17(9)

Conclusions: Incidence of HER2+ breast cancers is 14%, majority being EBCs (81%). Only 62% of the HER2+ EBC patients received Trastuzumab. Whilst the commonest reason for not receiving Trastuzumab is small node negative tumours (which is compatible with UK guidelines), an equal number of patients potentially missed optimal therapy for reasons not noted in the guidelines. Recent studies have demonstrated that being HER2+ is a significant risk factor for relapse in patients previously perceived to be at low risk and no HER2+ patient should now be considered low risk.[1]

Reference:

1. Tovey SM et al. Poor survival outcomes in HER2+ breast cancer patients with low-grade, node-negative tumours. *BJC* 2009;**100**(5):680–3.

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O-40 BREAST CANCER TREATMENT IN THE ELDERLY

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Objective: Of the 49,452 breast cancers diagnosed in the UK in 2006, 25,049 (51%) were diagnosed symptomatically in patients aged 50 and over. This study compares the nature and treatment of symptomatic invasive cancers in patients aged 50–69 and 70 years or over ('elderly').

Methods: Data were extracted from national audit databases and from the merged cancer registry database linked to HES.

Results: 84% of Patients aged 50–69 had surgery recorded compared with 55% of patients aged 70 or over. Surgery rates increased to 79% in 'elderly' patients known to be ER negative. 'Elderly' patients were more likely to have a mastectomy (61% versus 50%). For surgically treated tumours, prognostic factors were similar in both groups: node positivity: 54% in 50–69 versus 50% in 'elderly', ER status (73% ER positive in 50–69 versus 77% in 'elderly') and grade (52% Grade 1 or 2 in 50–69 versus 59% in 'elderly'). For cases with adjuvant therapy data available, radiotherapy after conserving surgery was slightly lower in the 'elderly' (87% versus 94%), chemotherapy for node positive patients was much lower in the 'elderly' (21% versus 75%) and more 'elderly' patients received hormone therapy (90% versus 83%).

Conclusion: 'Elderly' patients were less likely to receive surgery or chemotherapy. Patient choice, the presence of co-morbidities, lack of evidence on the relative risks/benefits of adjuvant therapy or reduced access to surgery for older patients are factors which might explain the differential treatment of these patients.

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O-41 AGE SPECIFIC BREAST CANCER RELATIVE SURVIVAL IN THE EAST OF ENGLAND

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Background: Breast cancer relative survival (BCRS) tends to be poorer in older women, but the reasons for this are not clear. We examined the influence of patient and tumour characteristics, and treatment on BCRS to see if these could explain the age specific effects.

Methodology: Data for 14,048 female breast cancer patients diagnosed from 1999 to 2007 aged 50 years or over were obtained from the Eastern Cancer Registration and Information Centre. We estimated relative 5- and 10-year survival for patients in four age groups (50–69, 70–74, 75–79, and 80+). We also modelled relative excess mortality rate (REM) adjusting for potential confounders. Covariates included in the analysis were age, TNM stage, histologic grade, ER status, mode of detection, volume at hospital of diagnosis, and treatment (surgery, radiotherapy, chemotherapy and hormonal therapy.

Results: Median follow-up time was 4.7 years. Relative 5-year survival was 90%, 81%, 76% and 68% for patients aged 50–69, 70–74, 75–79 and 80+, respectively. Corresponding relative 10-year survival was 84%, 77%, 66% and 60%. Similar patterns were seen for both ER+ and ER− and for low and high volume hospitals.

Unadjusted REM was 1.95, 2.86 and 4.30 for patients aged 70–74, 75–79 and 80+, respectively (50–69 reference). These were