Conclusions: Baseline post-surgery, pre-radiotherapy cosmesis is an important determinant of overall cosmesis at 2 years after radiotherapy. An important component of breast induration and shrinkage is actually due to surgery rather than radiotherapy. Larger breast volume, baseline surgical cosmesis, post-operative infection and smoking influence late radiotherapy toxicity. Modification of preventable risk factors such as post-operative infection and smoking may limit the development of late toxicity.

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O-50 TARGIT (TARGETED INTRA-OPERATIVE RADIOTHERAPY FOR EARLY STAGE BREAST CANCER): RESULTS FROM THE TARGIT A RANDOMIZED CONTROLLED TRIAL

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Background: After breast conserving surgery, 90% of recurrent cancer occurs within the index quadrant. Hence, restricting radiation therapy to the immediate area around the tumour bed after removal of the primary tumour may be adequate (Vaidya JS et al. Br J Cancer 1996;74:820–4).

Materials and methods: Using the technique of partial breast irradiation developed at UCL (Vaidya JS, Baum M, Tobias JS, et al. Ann Oncol 2001;12:1075–80) we launched the international TARGIT A randomized controlled trial in March 2000 comparing the policies of TARGIT versus standard whole breast external beam radiotherapy (EBRT) after breast conserving surgery with local recurrence as the main outcome measure (www.thelancet.com/protocol-reviews/99PRT-47). Accrual from 28 international centers reached 2232 in April 2010, with 80% power to detect a difference in relapse rate of 2.5% (the non-inferiority margin).

Results: Patient demographic and tumour characteristics are as follows: mean age 63 years (IQR 57–69), mean tumour size 12 mm (IQR 9–18 mm), N stage 17% +ve. We intend to present the unblinded data with an analysis of safety and efficacy.

Conclusions: If this analysis shows non-inferiority, then a clinically significant difference in early local recurrence between TARGIT and EBRT remains unlikely, making single session partial breast irradiation with TARGIT a plausible new standard of care in the near future.

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O-51 CLINICAL OUTCOME OF PATIENTS MANAGED IN A DEDICATED PRIMARY BREAST CANCER CLINIC FOR OLDER WOMEN (THE CLINIC)

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Background: The Clinic was established in 1973. Over the last decade, it has evolved into a combined surgical/oncology facility supported by dedicated breast care nurses. Also, surgery, with integral axillary staging, and adjuvant radiotherapy (RT) and systemic therapy have become standard for most patients though non-operative treatments (e.g. primary endocrine therapy (PET)) are used in others based on multi-disciplinary assessment in the Clinic. This study aimed to compare the clinical outcome across these periods.

Methods: Over 36 years (1973–2009), 1708 women $\geqslant$70 years with early operable primary breast cancer were managed in the Clinic according to a single set of clinical guidelines at any time point. Analysis was carried out based on retrospective review and continued update of patient records.

Results: As at 50-month median follow-up (maximum = 261):

	1973–1999	2000–2009	
N	917	791	
Treatment	*N* (%)	*N* (%)	
Surgery	392 (42.7)	446 (56.4)	
PET	510 (55.6)	324 (41.0)	
Primary RT	9 (1.0)	12 (1.5)	
No treatment	6 (0.7)	9 (1.1)	
Adjuvant endocrine therapy[a]	124 (31.7)	247 (55.5)	
Adjuvant RT[a]	15 (6.3)	155 (38.4)	
Outcome (% per annum)			*p*-value
Local recurrence[a]	2.2	0.5	<0.000
Regional recurrence[a]	1.8	0.4	<0.000
Contralateral cancer	0.7	0.4	0.091
Metastasis	2.9	1.9	<0.002
5-year breast cancer specific survival	80%	90%	<0.000
5-year overall survival	56%	68%	<0.000

[a] Surgery group only.

Conclusion: In this recent decade, while surgery became the predominant treatment, a significant proportion of patients (~40%) had non-operative therapies, selection of which was based on assessment in the Clinic. This management approach appears to produce excellent clinical outcome, which is significantly better than earlier period.

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O-52 EAST OF ENGLAND BREAST CANCER SURVIVAL CLOSE TO BEST IN EUROPE

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Background: The Eurocare-4 (2000–2002) period analysis documents a mean European age-adjusted 5-year relative breast cancer survival of 79% with higher individual figures for Finland (85.7%), Norway (84.1%) and Sweden (86.3%) (*Lancet Oncol 2007;8:784–96*). The corresponding mean figure for England was 77.8%. We now compare these predicted survival estimates with actual age-adjusted relative 5-year breast cancer overall survival for women diagnosed with invasive breast cancer in the East of England from 2000 to 2002.

Method: The East of England covers a population of 5.5 million people. Five-year age-adjusted relative breast cancer survival was calculated overall, and in specific age groups, for 10,787 women with invasive breast cancer diagnosed from 2000 to 2002 in the East of England for comparison with the results from the Eurocare-4 study.

Results:

Age-adjusted 5-year relative breast cancer survival in East of England for period 2000–2002.

Age group	Number of patients	Relative survival	95% CI
45–54	2563	87.5%	86.1–88.9
55–64	2945	89.5%	88.1–90.9
65–74	2335	83.9%	81.8–86.1
75+	2944	73.3%	70.1–76.4
All women	10,787	82.5%	81.4–83.6

Conclusion: These data confirm breast cancer survival rates for East of England that are close to European best figures for women aged 45–64. The mean survival of 82.5% for all women however is being reduced by worse survival in women aged 65+ and a strategy that ensures optimal breast cancer treatment for women in this age group should allow the mean survival to improve even further.

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O-53 A STUDY OF THE VALUE OF COMPREHENSIVE GERIATRIC ASSESSMENT (CGA) IN OLDER WOMEN WITH PRIMARY BREAST CANCER – PRELIMINARY RESULTS

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Background: Despite being an important health issue, breast cancer in older women is under-researched. This study aimed to identify how CGA may be linked to treatment decision making.

Methods: Women ⩾70 years with newly diagnosed primary breast cancer in Nottingham were invited to take part. Decision for a particular treatment was made between the clinical team and the patient, and this was not part of the study. Each patient then completed an established CGA tool – a multi-dimensional questionnaire incorporating information on demographics, mood, social activities and support, medication, functional status, cognition, nutritional state and co-morbidities.

The study is ongoing. At this preliminary analysis, 20 patients (aged 70–87) were recruited from different treatment groups (mastectomy $n = 8$, breast conserving surgery, $n = 4$, primary endocrine therapy (PET) $n = 7$, primary radiotherapy $n = 1$).

Results: Compared to patients undergoing surgery, the PET group was found to be older (median age 85 versus 76). Patients on PET also reported having lower median physical functioning (7.5 versus 11.5) and social support (66.67 versus 89.95) scores, mood levels (67.65 versus 85.29) and more co-morbidities (median 4 versus 2).

Conclusions: Using a CGA tool may be beneficial in guiding treatment decision. This ongoing study may establish a tool specific to the context of older women with primary breast cancer. This could then become part of routine consultation and may help identify patients who would require input of a geriatrician. When combined with quality of life measures and biological information, there is potential to provide a holistic approach to this under-served population.

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O-54 INVOLVEMENT OF MiR-34A IN RESISTANCE OF BREAST CANCER CELLS TO DOCETAXEL

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Introduction: Understanding the mechanisms of drug resistance is important to improve and deliver effective therapy. MicroRNAs (miRNA) are small RNA molecules that regulate gene expression, hence we hypothesised that gene silencing, by altered miRNA expression, causes docetaxel resistance.

Methods: Quantitative PCR-based miRNA arrays were used to examine the role of miRNAs in acquired resistance of breast cancer cells (MCF-7 and MDA-MB-231) to docetaxel. Quantitative PCR and western analysis were used to measure target gene mRNA and protein expression, respectively. MicroRNA expression was modulated and docetaxel response was measured by cell viability assay.

Results: We found 299 and 226 miRNAs altered in MCF-7 and MDA-MB-231 docetaxel-resistant cells, respectively. Only miRNA alterations that reached statistical significance, which targeted experimentally validated genes involved in cell cycle, apoptosis or drug resistance, were selected for further investigation. Docetaxel resistance was associated with increased expression of miR-34a and miR-141 and decreased expression of miR-7, miR-16, miR-30a, miR-125a-5p, miR-126 and miR-429. Computational target prediction revealed 11 candidate genes targeted by these miRNAs. Quantitative PCR and western analysis confirmed decreased expression of only two genes, BCL2 and cyclinD1, in docetaxel-resistant cells, which are both targeted by miR-34a. Inhibition of miR-34a enhanced response to docetaxel in MCF-7 docetaxel-resistant cells whereas overexpression of miR-34a conferred resistance in MCF-7 docetaxel-sensitive cells. Modulation of miR-34a expression was correlated with expected BCL2 and cyclinD1 protein expression changes.