emitted from a point source, delivering a dose of radiation (~20 Gy at the surface and ~5 Gy at 1 cm) directly to the tumour bed. The women could then proceed to have chemotherapy and/or adjuvant hormonal therapy as required. In addition, patients who were deemed unfit for surgery (n = 3) received interstitial radiotherapy alone under local anaesthetic. Women were followed-up for local recurrence.

Results: Over the past 7 years in centres in 3 countries (UK, Germany and Australia), 77 patients have been treated in this way, with median age of 66 (56−77 IQR) years and a median follow-up of 37 (25−54 IQR) months. To date there have been two local recurrences, which gives an estimated annual local recurrence rate of 0.78% (95% CI 0.09% to 2.77%).

Conclusion: This cohort adds to the evidence that targeted radiotherapy using IORT offers a safe and effective method of delivering radiotherapy to breast cancer patients in whom EBRT is not feasible or is not an option.

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Pragmatism in the TARGIT trial encouraged wider participation of centres yet yielded an unexpected homogeneous patient profile

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In 1999, we designed a randomised controlled trial to test whether TARGeted Intraoperative radioTherapy (TARGIT) was equivalent to post-operative external beam radiotherapy (EBRT).

To cater for a wide level of equipoise, our design was pragmatic with minimal restrictions for age ($\geqslant$45) and tumour size (preferably smaller than 3.5 cm), and no restrictions for grade and nodal status. At the outset, each centre specified these options in a treatment policy document.

This analysis of the treatment policies includes 1674 patients from 24 centres ransomised until April 2009. The minimum age at entry was specified to be 40, 45/48, and 50 by 2, 8 and 14 centres that randomised 243 (14.5%), 514 (30%) and 917 (55%) patients. However, 1566 (93.5%) of patients randomised were $\geqslant$50; 45−49y = 83 (5%) and 40−44y = 21 (1.25%). 10 (525 patients) centres did not restrict tumour size while 8 (800 patients), 1 (187 patients), 5 (152 patients) centres restricted the size to $\leqslant$2 cm, $\leqslant$2.5 cm, $\leqslant$3 cm. However, 84% patients had tumour size $\leqslant$2 cm and <4% were >3.5 cm. Grade 3 was excluded by only 4 centres (278 (16.6%) patients), but only 13% of all randomised patients had grade 3 cancers.

TARGIT could also be delivered either as a first or second procedure, and 37% more patients were randomised because of this. Furthermore, if patients randomised and given intraoperative radioatherapy were found to be high risk of elsewhere-recurrence (e.g. lobular cancers or EIC or other prespecified features) EBRT could be added within the protocol which essentially tested the two strategies and not techniques. Only 10% patients randomised to IORT received additional EBRT.

Allowing clinicians to be liberal in their intended inclusion criteria increased appeal and encouraged wider participation, yet led to a relatively homogeneous patient sample, demonstrating an unexpected conservatism in this pragmatic trial.

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Accelerated partial breast irradiation (APBI) after breast conserving surgery − early tolerance, dosimetric and volumetric parameters of interstitial multicatheter implant

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Purpose: The aim of the study was to analyze early tolerance and dosimetric and volumetric quality of interstitial multicatheter implant in Accelerated Partial Breast Irradiation (APBI) in select early stage breast cancers following BCT.

Materials/Methods: From May 2006 to October 2009 in Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch 60 patients with preinvasive ductal breast cancer (DCIS − 7 women) or invasive ductal breast cancer (53 women) were selected to prospective Phase II trial. The mean age was 62 years (range 45−80 yrs). All women underwent mammography, usg and MRI for breast to exclude multicentrcity and multifocality. In all cases postoperative specimen histopathology was classified as pT1N0 with a pathologically negative margin (margins from 2 to 15 mm). One patient received adjuvant systemic chemotherapy (AC 4 cycle), the others received adjuvant hormonotherapy. APBI treatment was delivered with High Dose Rate Brachytherapy. Treatment planning was based on CT. Catheters were inserted in local anaesthesia. Median number of catheters 14 (range 10−18). All women received total dose 32 Gy (fractionation dose 4 Gy twice a day, in first and last day only one fraction) in 5 days.

Results: The mean follow-up period from the beginning of treatment was 18 months (range from 7 to 40 months). Median V100 − 91.12 cm^3, median V200 − 9.76 cm^3. D10 and D2 for lung was 18% and 29% referent dose, respectively. Maximal dose on the skin surface was 44.7% (range 19% to 67%).

Early complications: 21 patients (35%) had bruises after catheters implantation and 2 women (3.3%) experienced implant infection (dermatitis) treated with antibiotics. In 6 cases antibiotics were used as a prophylaxis (10%).

Conclusions: Multicatheter HDR APBI, in selected subgroup of patients, has good early tolerance and good dosimetric and volumetric quality of implant. Longer follow-up and randomized trials are necessary.

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Effect of breathing on contralateral breast doses in patients with breast carcinoma receiving radiotherapy

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Background and Purpose: Radiotherapy (RT) for breast cancer results in scattered radiation doses to the contralateral breast which is found to be associated with an increased risk of secondary malignancy. This prospective study investigates the dosimetric and volumetric changes in contralateral breast as a consequence of breathing cycle.

Methods and Patients: Ten patients with left breast carcinoma underwent breast conservative surgery or mastectomy receiving RT (breast or chest wall and regional lymph nodes) are included. All patients were positioned supine on breast board and a body cast was fabricated for shoulder and trunk immobilization. For this study, planning CT (computerized tomography) images were obtained during deep inspiration (I) and end of expiration (E), besides free breathing (FB) in order to simulate the changes during respiratory cycle. CT images were taken in the treatment position on a flat table top for 3 different series: during FB, I and E, with 3 mm intervals. I and E images were registered to FB using rigid bony anatomy references. Targets and contralateral breast volumes were contoured by the same Radiation Oncologist on 3 different image series. Three dimensional conformal or intensity modulated RT planning was done to obtain dose-volume information using 3 different CT series. Treatment plans and dose calculations were constructed using CT images taken during free breathing. Then, plan was exported to I and E image series. No changes in the initial FB scan treatment plan such as gantry angles, number of monitor units delivered per beam were permitted. The significance of dose and volume changes was investigated with "repeated measures ANOVA" test.

Results: Maximum contralateral breast dose to a 2 cc volume was higher for I, then FB and E for all patients. Median values for maximum contralateral breast dose to a 2 cc volume for FB, I and E were 284 cGy (127–1458 cGy), 353.5 cGy (231–5709 cGy) and 294 cGy (137–4264 cGy) respectively ($p = 0.2$). Median values for volume (cc) receiving more than 100 cGy for FB, I and E were 74 cc (14–445 cc), 108 cc (53–650 cc) and 72 cc (17–650 cc), respectively ($p = 0.1$). However, contralateral breast dose and volume variations during breathing were not found to be statistically significant.

Conclusion: Results of this study suggest that there are variations in contralateral breast volume and dose; however these differences are not statistically significant. This can be further investigated especially in left breast cancer patients where contralateral breast dose might be sacrificed in order to limit the dose to heart and its components.

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Prospective trial for Japanese breast cancer patients treated with accelerated hypofractionated whole breast irradiation for breast conserving treatment

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Background: Randomized controlled trials have demonstrated that breast irradiation after lumpectomy substantially reduces recurrence of cancer in the breast and thereby increases the likelihood of breast conservation. Though there were several trials with hypofractionated whole breast irradiation, few patients enrolled in the trials. In Japan, the most commonly

used schedule for whole breast irradiation after breast concerving surgery is 2 Gy daily fractions given 5 times a week to a total dose of 50 Gy over 5 weeks with the optional addition of a boost to the primary site to 10 Gy in 5 daily fractions over 1 week. We present our clinical trial utilizing radiation therapy to deliver accelerated hypofractionated whole breast irradiation in patients with early-stage breast cancer treated with breast conserving therapy.

Methods and Materials: Between March 2002 and March 2003, 70 patients with Stage 0−3 breast cancer were enrolled at National Cancer Center Hospital, Japan, institutional review board-approved. Eligibility criteria included invasive ductal and lobular histologies as well as ductal carcinoma in situ, lumpectomy, and written patients consent. The prescribed dose was 40 Gy in 16 fractions given over 3 weeks to whole breast using 4MV or 6MV X-ray. Addition of a boost to the primary site to 10 Gy in 5 daily fractions over 1 week was delivered patients with closed surgical margin (<5 mm). All patients were treated once a day.

Table: Patients and tumor characteristics

Characteristic	
Median age (range)	54 yrs (30−76)
Clinical stage	
0	7 patients
1	24
2	33
3	3
Pathohistology	
Intraductal carcinoma	7 patients
Invasive ductal carcinoma	53
Others	7
Median pathological tumor size (range)	19 mm (5−67)
Surgical margin	
Negative	45 patients
Close or positive	22
Axillar dissection	
yes	60 patients
Sentinel lymph nodes biopsy	
Yes	6
No	1
Lymph node metastasis	
no	62 patients
1−3	7
4−	0
Grade	
1	8 patients
2	36
3	23
Estrogen receptor status	
Positive	48 patients
Negative	19
Systemic chemotherapy	
No	46 patients
Preoperative	8
Postoperative	13
Hormone therapy	
No	47 patients
Yes	20

Results: The median follow-up after radiotherapy was 85 months (range, 3−92 months). 3 patients without protocol treatment were excluded the analysis.

Baseline characteristics including age, tumor size, estrogen receptor status, tumor grade etc were presented in table.

Three patients experienced a local breast cancer recurrence as a first event.

At 7 years, local recurrence-free survival was 94.4%. Any recurrence was noted as a first event − 11 events were identified. (3 local recurrences, 2 regional recurrences, and 6 distant recurrences). At 7 years, disease-free survival rate was 82.3%. At 7 years, overall survival rate was 98.3%.

In late radiation toxicity of the subcutaneous tissue, no grade 2, 3 was observed. Incidence of grade 0 was 70% and grade 1 was 30%. No skin telangiectasia was observed. One patient developed rib fracture at 23 months.

Conclusion: Hypofractionated whole breast irradiation for breast conserving therapy is a highly effective and safe treatment for Japanese women.

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Prognostic factors in patients treated with radiotherapy for bone metastasis from breast carcinoma

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Background: The aim of this study was to evaluate prognostic factors and to analyze the overall survival of patients with bone metastasis due to breast carcinoma.

Materials/Methods: We performed a retrospective review of 137 patients with bone metastasis (BM) from breast cancer who were treated with radiotherapy (RT) between 1999–2008. All patients had histologically confirmed breast cancer. Median age was 49 (range 26−83). At the time of BC diagnosis: 72 (53%) patients were premenopausal, 64 (47%) were postmenopausal. ER+, PR+ and HER2 phenotypes were represented by 67%, 64%, 69% of this group, respectively. Fourty patients (29%) had one bone metastasis, 25 (18%) had two, 14 (10%) had three and 58 (42%) had more than four bone metastases. Due to first bone metastases, RT was mostly applied to thoracal vertebra region (26%). Most patients (80%) had received a total dose of 30 Gy in fractions of 3 Gy.

Results: Median follow-up was 57 (3–279) months. At the time of analysis, 65 patients had died with disease, 72 were alive. The median time from BC to BM was 35 (1–192) months. The median overall survival after diagnosis of bone metastasis was 43 months. Overall survival rate at 2 and 5 years was 87% and 63%, respectively. Age, menopausal status, clinical stage, Karnofsky performance status, grade, ER, PR and HER-2/neu status, alkaline phosphatase (ALP) and calcium levels, RT fields, number of bone metastases, the presence of distant metastasis before BM and interval from BC diagnosis to BM were investigated as a prognostic factors. Univariate and multivariate analysis demonstrated that ER, PR, HER-2/neu and ALP level in serum were statistically significant predictors of survival.

Conclusions: This study demostrated that ER, PR positivity and HER-2/neu negativity and low level of ALP were significantly associated with better survival in bone metastasis due to breast carcinoma.

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Four times weekly adjuvant breast radiotherapy with a moderately intensified boost to the tumour bed − feasibility and acute toxicity

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Background: Standard safe schedules for adjuvant breast radiotherapy (RT) after breast conserving surgery use a dose of 45−54 Gy with fraction doses of 1.8−2.5 Gy in an overall treatment time of 35−38 days to the whole breast [1]. A boost of 16 Gy to the tumor bed improves local control but leads to increased fibrosis in the boost area [2]. The optimal dose and technique for the boost remain unclear. Biological considerations such as the low α/β ratio in breast cancer [3−5] and accelerated proliferation as well as the possibility of selecting resistant residual tumor cells are in favour of a dose intensification of the boost after whole breast RT (WBI). We chose a moderate intensification to avoid fibrosis and hypothesize that four times weekly adjuvant breast RT with a moderately intensified boost to the tumour bed is feasible and yields acceptable acute toxicity in patients $\leqslant$70 years.

Material and Methods: 50 consecutive patients $\leqslant$70 years with ductal carcinoma in situ or pT1−2 (ypT0included) pN0−1 invasive breast cancer after breast conserving surgery with or without chemotherapy and/or hormonotherapy were studied. Treatment consisted of 21×2.25 Gy WBI followed by a boost of 6×2.5 Gy to the tumor bed during $6\frac{1}{2}$ weeks by two tangential photon beams (6−18 MV) for WBI and photon or electron beams for the boost depending on tumour location. Acute RTOG-EORTC skin toxicity in the breast and the boost region was assessed weekly during treatment and six weeks after the end of RT.

Results: The median age of the patients was 57 (33−69) years. Seven patients had ductal carcinoma in situ, 43 patients invasive carcinoma. Median overall treatment time was 44 (42−46) days. Acute G1, G2 and G3 skin toxicity occurred in 13 (26%), 30 (60%) and seven patients (14%) in the boost region and in 18 (36%), 30 (60%) and two patients (4%) outside the boost. At a median follow-up of six weeks after the end of RT, remission of skin toxicity ($\leqslant$G1) was seen in all but two patients with G2 toxicity.

Conclusions: On the basis of biological considerations and promising results of hypofractionated schedules [6−9], an intensified boost to the tumour bed after WBI may improve local control. Our schedule using four times weekly WBI followed by a moderately intensified boost to the tumour bed is feasible and well tolerated at short term in patients $\leqslant$70 years